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FILE LAST UPDATED: 9 Aug 2006 (20060809/ED)

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L1 558 SEA FILE=CAPLUS ABB=ON BRANDT J?/AU
L2 152 SEA FILE=CAPLUS ABB=ON FARID N?/AU
L3 261 SEA FILE=CAPLUS ABB=ON JAKUBOWSKI J?/AU
L4 89 SEA FILE=CAPLUS ABB=ON WINTERS K?/AU
L5 2 SEA FILE=CAPLUS ABB=ON L1 AND L2 AND L3 AND L4

*Inventor
search*

=> fil medl jic wpix biosis embase; d que l13; d que l14; s l13 or l14
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L8 2404 SEA BRANDT J?/AU
L9 772 SEA FARID N?/AU
L10 629 SEA JAKUBOWSKI J?/AU
L11 371 SEA WINTERS K?/AU
L13 3 SEA L8 AND L9 AND L10 AND L11

L8 2404 SEA BRANDT J?/AU
L9 772 SEA FARID N?/AU

L10 629 SEA JAKUBOWSKI J?/AU
L11 371 SEA WINTERS K?/AU
L12 55838 SEA PERCUTANEOUS?(5A) CORONARY
L14 16 SEA (L8 OR L9 OR L10 OR L11) AND L12

L15 18 L13 OR L14

=> dup rem l5,l15

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PROCESSING COMPLETED FOR L15

L16 13 DUP REM L5 L15 (7 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE CAPLUS
ANSWERS '3-7' FROM FILE MEDLINE
ANSWERS '8-13' FROM FILE BIOSIS

=> d ibib ed abs 1-2; d iall 3-13

L16 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2006:366820 CAPLUS

TITLE: The Platelet Inhibitory Effects and Pharmacokinetics
of Prasugrel After Administration of Loading and
Maintenance Doses in Healthy Subjects

AUTHOR(S): Jakubowski, Joseph A.; Payne, Christopher
D.; Brandt, John T.; Weerakkody, Govinda J.;
Farid, Nagy A.; Small, David S.; Naganuma,
Hideo; Li, Grace Ying; Winters, Kenneth J.

CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company,
Indianapolis, IN, 46285, USA

SOURCE: Journal of Cardiovascular Pharmacology (2006), 47(3),
377-384

CODEN: JCPCDT; ISSN: 0160-2446

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 21 Apr 2006

AB Prasugrel (CS-747, LY640315), a novel thienopyridine, is a potent and orally active antiplatelet agent in vivo. The aims of this double-blind, double-dummy, placebo-controlled, randomized, parallel group phase 1 study were to investigate the antiplatelet effects of prasugrel after oral administration of a loading dose (LD) and subsequent 20 days of once-daily maintenance dosing (MD), to characterize the pharmacokinetics of prasugrel metabolites with an LD/MD regimen, and to assess the safety and tolerability of prasugrel in healthy subjects. Subjects were randomly

assigned in a 1:1:1 ratio to prasugrel 40 mg LD/7.5 mg MD (n=11), prasugrel 60 mg LD/15 mg MD (n=10), or placebo LD/placebo MD (n=11). Prasugrel 40 and 60 mg LDs provided rapid and consistent inhibition of 20 μ M ADP-stimulated platelet aggregation. Prasugrel 7.5 and 15 mg MDs maintained inhibition in a dose-dependent manner. The pharmacokinetic data indicate that exposure to prasugrel metabolites occurs rapidly after dosing and is consistent with dose proportionality. Within the limitations of this study, the safety and tolerability results suggest that prasugrel is well tolerated when dosed as an initial LD followed by a lower daily MD for 20 days. Prasugrel LDs and MDs provide rapid and sustained inhibition of ADP-mediated platelet aggregation.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2004:996025 CAPLUS

DOCUMENT NUMBER: 141:428013

TITLE: 2-Acetoxy-5-(α -cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine pharmaceuticals for treating cardiovascular disease

INVENTOR(S): Brandt, John Thomas; Farid, Nagy
Alphonse; Jakubowski, Joseph Anthony;
Winters, Kenneth John

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

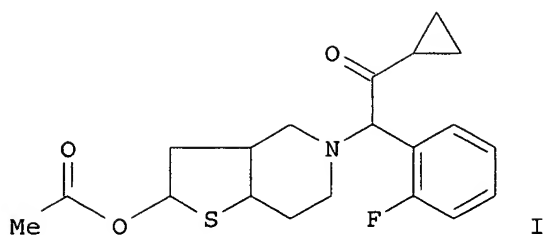
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098713	A2	20041118	WO 2004-US11257	20040426
WO 2004098713	A3	20041229		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1660183	A2	20060531	EP 2004-750031	20040426
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK			
PRIORITY APPLN. INFO.:			US 2003-467903P	P 20030505
			WO 2004-US11257	W 20040426

ED Entered STN: 19 Nov 2004

GI



AB A method of treating cardiovascular diseases comprising administering I or a pharmaceutically acceptable salt, solvate, prodrug, active metabolite, racemate or enantiomer thereof, in conjunction with coronary and non-coronary intervention procedures is disclosed. I was prepared and formulated into tablets or capsules.

L16 ANSWER 3 OF 13 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 2005331652 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 15967851
 TITLE: Randomized comparison of prasugrel (CS-747, LY640315), a novel thienopyridine P2Y₁₂ antagonist, with clopidogrel in **percutaneous coronary** intervention: results of the Joint Utilization of Medications to Block Platelets Optimally (JUMBO)-TIMI 26 trial.
 AUTHOR: Wiviott Stephen D; Antman Elliott M; **Winters Kenneth** J; Weerakkody Govinda; Murphy Sabina A; Behounek Bruce D; Carney Robert J; Lazzam Charles; McKay Raymond G; McCabe Carolyn H; Braunwald Eugene
 CORPORATE SOURCE: TIMI Study Group, Cardiovascular Division, Brigham and Women's Hospital, Department of Medicine, Harvard Medical School, Boston, Mass 02115, USA. (JUMBO-TIMI 26 Investigators). swiviott@partners.org
 SOURCE: Circulation, (2005 Jun 28) Vol. 111, No. 25, pp. 3366-73. Electronic Publication: 2005-06-20. Journal code: 0147763. E-ISSN: 1524-4539.
 COMMENT: Comment in: Evid Based Cardiovasc Med. 2005 Dec;9(4):301-4. PubMed ID: 16380060
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (CLINICAL TRIAL, PHASE II)
 Journal; Article; (JOURNAL ARTICLE)
 (RANDOMIZED CONTROLLED TRIAL)
 (CLINICAL TRIAL)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 200602
 ENTRY DATE: Entered STN: 29 Jun 2005
 Last Updated on STN: 4 Feb 2006
 Entered Medline: 3 Feb 2006

ABSTRACT:
 BACKGROUND: Despite the current standard antiplatelet regimen of aspirin and clopidogrel (with or without glycoprotein IIb/IIIa inhibitors) in *****percutaneous*** coronary** intervention patients, periprocedural and postprocedural ischemic events continue to occur. Prasugrel (CS-747, LY640315), a novel potent thienopyridine P2Y₁₂ receptor antagonist, has the potential to achieve higher levels of inhibition of ADP-induced platelet

aggregation than currently approved doses of clopidogrel. **METHODS AND RESULTS:** Joint Utilization of Medications to Block Platelets Optimally-Thrombolysis In Myocardial Infarction 26 (JUMBO-TIMI 26) was a phase 2, randomized, dose-ranging, double-blind safety trial of prasugrel versus clopidogrel in 904 patients undergoing elective or urgent **percutaneous coronary** intervention. Patients were randomized to either standard dosing with clopidogrel or 1 of 3 prasugrel regimens. Subjects were monitored for 30 days for bleeding and clinical events. The primary end point of the trial was clinically significant (TIMI major plus minor) non-CABG-related bleeding events in prasugrel- versus clopidogrel-treated patients. Hemorrhagic complications were infrequent, with no significant difference between patients treated with prasugrel or clopidogrel in the rate of significant bleeding (1.7% versus 1.2%; hazard ratio, 1.42; 95% CI, 0.40, 5.08). In prasugrel-treated patients, there were numerically lower incidences of the primary efficacy composite end point (30-day major adverse cardiac events) and of the secondary end points myocardial infarction, recurrent ischemia, and clinical target vessel thrombosis. **CONCLUSIONS:** In this phase 2 study, which was designed to assess safety when administered at the time of **percutaneous coronary** intervention, prasugrel and clopidogrel both resulted in low rates of bleeding. The results of this trial serve as a foundation for the large phase 3 clinical trial designed to assess both efficacy and safety.

CONTROLLED TERM: Check Tags: Female; Male

Adolescent

Adult

Aged

***Angioplasty, Transluminal, Percutaneous Coronary: AE, adverse effects**

Angioplasty, Transluminal, Percutaneous Coronary: MT, methods

Cardiovascular Diseases: PC, prevention & control

Comparative Study

Dose-Response Relationship, Drug

Double-Blind Method

Hemorrhage: CI, chemically induced

Humans

Incidence

***Membrane Proteins: AI, antagonists & inhibitors**

Middle Aged

***Piperazines: AD, administration & dosage**

Piperazines: TO, toxicity

***Platelet Aggregation Inhibitors: AD, administration & dosage**

Platelet Aggregation Inhibitors: TO, toxicity

Pyridines: AD, administration & dosage

Pyridines: TO, toxicity

***Receptors, Purinergic P2: AI, antagonists & inhibitors**

Research Support, Non-U.S. Gov't

***Thiophenes: AD, administration & dosage**

Thiophenes: TO, toxicity

Ticlopidine: AD, administration & dosage

***Ticlopidine: AA, analogs & derivatives**

Ticlopidine: TO, toxicity

CAS REGISTRY NO.: 55142-85-3 (Ticlopidine); 90055-48-4 (clopidogrel)

CHEMICAL NAME: 0 (Membrane Proteins); 0 (P2RY12 protein, human); 0 (Piperazines); 0 (Platelet Aggregation Inhibitors); 0 (Pyridines); 0 (Receptors, Purinergic P2); 0 (Thiophenes); 0 (prasugrel); 0 (purinoceptor P2Y12); 0 (thienopyridine)

L16 ANSWER 4 OF 13

MEDLINE on STN

DUPLICATE 4

ACCESSION NUMBER:

97057313

MEDLINE

DOCUMENT NUMBER: PubMed ID: 8901652
TITLE: Association of heparin-resistant thrombin activity with acute ischemic complications of coronary interventions.
AUTHOR: Oltrona L; Eisenberg P R; Lasala J M; Sewall D J; Shelton M E; Winters K J
CORPORATE SOURCE: II Divisione Cardiologica, Ospedale Niguarda, Milano, Italy.
CONTRACT NUMBER: HL-17646 (NHLBI)
SOURCE: Circulation, (1996 Nov 1) Vol. 94, No. 9, pp. 2064-71. Journal code: 0147763. ISSN: 0009-7322.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 6 Feb 1998
Entered Medline: 6 Dec 1996

ABSTRACT:

BACKGROUND: Acute thrombosis is thought to contribute to abrupt ***coronary*** occlusion during **percutaneous coronary** revascularization despite the administration of heparin and aspirin. This study was designed to detect the presence of heparin-resistant thrombin activity and to define its relationship to the acute ischemic complications of coronary interventions. METHODS AND RESULTS: Plasma levels of fibrinopeptide A (FPA) and prothrombin fragment 1.2 (F1.2), markers of thrombin and factor Xa activity, respectively, were measured in the coronary sinus with heparin-bonded catheters in 58 patients undergoing coronary interventions. Activated coagulation times were maintained > 300 seconds by the Hemochron method. Mean FPA levels decreased significantly, from 7.0 +/- 0.9 nmol/L before the procedure to 5.2 +/- 0.5 nmol/L after the heparin bolus and to 2.9 +/- 0.2 nmol/L after the procedure (P = .0001). In 26 patients (45%), FPA levels remained above the threshold for suppression angioplasty of thrombin activity determined during angiography in 7 patients without coronary artery disease (> 3.0 nmol/L). FPA concentrations after coronary interventions were increased in patients with intracoronary thrombus (P = .01), abrupt coronary occlusion (P = .06), postprocedural non-Q-wave myocardial infarction (P = .04), and clinically unsuccessful procedures (P = .04). F1.2 levels were relatively low before the procedures and did not change significantly. CONCLUSIONS: Heparin administration suppresses thrombin activity in most but not all patients undergoing coronary interventions. Heparin-resistant thrombin activity is associated with angiographic evidence of intracoronary thrombus and ischemic complications of coronary interventions.

CONTROLLED TERM: Check Tags: Female; Male
Acute Disease
Aged
Angiography
Blood Specimen Collection
Factor Xa: AI, antagonists & inhibitors
Fibrinopeptide A: ME, metabolism
*Heart Catheterization: AE, adverse effects
*Heparin: PD, pharmacology
Humans
Middle Aged
*Myocardial Ischemia: CO, complications
Myocardial Ischemia: ET, etiology
Myocardial Ischemia: ME, metabolism
Peptide Fragments: ME, metabolism
Prothrombin: ME, metabolism
Reproducibility of Results

Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
*Thrombin: AI, antagonists & inhibitors
*Thrombin: ME, metabolism
Thrombosis: DT, drug therapy
Thrombosis: ET, etiology
Whole Blood Coagulation Time

CAS REGISTRY NO.: 25422-31-5 (Fibrinopeptide A); 9001-26-7 (Prothrombin);
9005-49-6 (Heparin)
CHEMICAL NAME: 0 (Peptide Fragments); 0 (prothrombin fragment 1.2); EC
3.4.21.5 (Thrombin); EC 3.4.21.6 (Factor Xa)

L16 ANSWER 5 OF 13 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 85254899 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3160477
TITLE: Failure of **percutaneous** transluminal
coronary angioplasty to stimulate platelet and
prostaglandin activity.
AUTHOR: Stine R A; Magorien R D; Bush C A; Kolibash A J; Leier C V;
Fertel R H; **Brandt J**; Unverferth D V
SOURCE: Catheterization and cardiovascular diagnosis, (1985) Vol.
11, No. 3, pp. 247-54.
Journal code: 7508512. ISSN: 0098-6569.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198508
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 26 Aug 1985

ABSTRACT:

Platelet function and prostaglandin activity were evaluated in nine patients with **coronary** artery disease undergoing **percutaneous** left anterior descending **coronary** artery angioplasty (PTCA) and compared to nine normal controls. Transcoronary measurements (arterial-coronary sinus) of platelet counts, mean platelet volume, platelet factor 4 (PF4), beta thromboglobulin, thromboxane (B2), and 6-keto-PGF 1 alpha were made. When compared to normal controls, the patients with coronary artery disease had higher circulating baseline levels of PF4 in the coronary sinus. There was no transcardiac production of any factor at baseline or immediately after infusion of nitroglycerin or performance of PTCA. These results suggest that PTCA does not grossly alter arachidonic acid metabolism or platelet activity.

CONTROLLED TERM: 6-Ketoprostaglandin F1 alpha: BL, blood
Adult
Aged
*Angioplasty, Balloon
Coronary Disease: BL, blood
*Coronary Disease: TH, therapy
Heart Catheterization
Humans
Middle Aged
*Platelet Aggregation
Platelet Count
Platelet Factor 4: PH, physiology
*Prostaglandins: BL, blood
Research Support, Non-U.S. Gov't
Thromboxane B2: BL, blood
beta-Thromboglobulin: ME, metabolism
CAS REGISTRY NO.: 37270-94-3 (Platelet Factor 4); 54397-85-2 (Thromboxane

CHEMICAL NAME: B2); 58962-34-8 (6-Ketoprostaglandin F1 alpha)
0 (Prostaglandins); 0 (beta-Thromboglobulin)

L16 ANSWER 6 OF 13 MEDLINE on STN
ACCESSION NUMBER: 1999030710 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9812911
TITLE: Effects of beta3-integrin blockade (c7E3) on the response
to angioplasty and intra-arterial stenting in
atherosclerotic nonhuman primates.
AUTHOR: Deitch J S; Williams J K; Adams M R; Fly C A; Herrington D
M; Jordan R E; Nakada M T; Jakubowski J A; Geary
R L
CORPORATE SOURCE: Departments of Surgery and Comparative Medicine, Wake
Forest University School of Medicine, Winston-Salem, NC,
USA.
CONTRACT NUMBER: HL49488 (NHLBI)
P01-HL45666 (NHLBI)
R01-HL57557 (NHLBI)
SOURCE: Arteriosclerosis, thrombosis, and vascular biology, (1998
Nov) Vol. 18, No. 11, pp. 1730-7.
Journal code: 9505803. ISSN: 1079-5642.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 15 Jan 1999
Last Updated on STN: 15 Jan 1999
Entered Medline: 10 Dec 1998

ABSTRACT:

Because the beta3-antagonist abciximab (c7E3 Fab) has significantly improved late outcomes after coronary angioplasty, the beta3 integrins have been implicated in the arterial response to injury. However, the mechanisms underlying this benefit are unknown. The observation that c7E3 binds beta3 integrins on vascular cells (alpha v beta3) with affinity equal to that for the platelet glycoprotein IIb/IIIa integrin has led to the hypothesis that c7E3 may act directly on the artery wall to prevent restenosis after angioplasty. To test this hypothesis, we studied the effects of c7E3 on structural changes within the artery wall after angioplasty or stent angioplasty in 23 male cynomolgus monkeys with established atherosclerosis. Animals were randomly assigned to receive either a bolus of c7E3 (0.4 mg/kg IV, n=11) followed by a 48-hour infusion (0.2 microg. kg-1. min-1) or an equal volume of vehicle (n=12). Animals received weight-adjusted aspirin and heparin and then underwent unilateral iliac artery experimental angioplasty and subclavian artery stent angioplasty (Palmaz). Iliac artery lumen diameter (LD) was determined by angiography at baseline (LDPre), after angioplasty (LDPost), and 35 days later (LDDay35). Arteries were then fixed by perfusion and removed for analysis. Lumen, intima, media, and external elastic lamina (EEL) areas were measured in iliac artery cross sections. Values from each injured iliac artery were normalized to the contralateral uninjured iliac artery to control for interanimal variability in baseline artery size and atherosclerosis extent. Intimal area was also measured in subclavian stent cross sections. c7E3 blocked platelet aggregation and prolonged the bleeding time from 2.8+/-1.1 to 19.8+/-2.5 minutes, P<0.001. Experimental angioplasty increased LDPost an average of 28%, and the initial gain was similar in both groups (P=NS). Despite an anti-platelet effect, c7E3 did not inhibit iliac lumen narrowing (LDDay35-LDPost: c7E3, -0.69+/-0.17 versus vehicle, -0.99+/-0.17 mm, P=0.35); intimal hyperplasia (neointima area: c7E3, 1.12+/-0.28 versus vehicle, 1.22+/-0.20 mm², P=0.77); or decrease in artery wall size (EEL area [percent of uninjured control]: c7E3, 101+/-7% versus vehicle, 121+/-7%). Stent intimal

hyperplasia was also unaltered by c7E3 treatment (neointimal area: c7E3, 1.09+/-0.16 versus vehicle, 1.28+/-0.11 mm², P=0.36). These results suggest that the benefits of c7E3 treatment in coronary angioplasty were not from inhibition of intimal hyperplasia or improved artery wall remodeling. Alternative mechanisms should be explored to explain improved late outcomes after angioplasty in patients treated with c7E3.

CONTROLLED TERM: Check Tags: Male

*Angioplasty, Transluminal, Percutaneous Coronary
Animals

*Antibodies, Monoclonal: TU, therapeutic use
Arteries

*Arteriosclerosis: TH, therapy

Blood Coagulation: DE, drug effects

Combined Modality Therapy

Drug Evaluation, Preclinical

Hematologic Tests

Hyperplasia: DT, drug therapy

*Immunoglobulin Fab Fragments: TU, therapeutic use

*Integrins: AI, antagonists & inhibitors

Lipids: BL, blood

Macaca fascicularis

*Platelet Aggregation Inhibitors: TU, therapeutic use

Research Support, Non-U.S. Gov't

Research Support, U.S. Gov't, P.H.S.

Stents

Treatment Outcome

CAS REGISTRY NO.: 143653-53-6 (abciximab)

CHEMICAL NAME: 0 (Antibodies, Monoclonal); 0 (Immunoglobulin Fab
Fragments); 0 (Integrins); 0 (Lipids); 0 (Platelet
Aggregation Inhibitors)

L16 ANSWER 7 OF 13 MEDLINE on STN

ACCESSION NUMBER: 95216989 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7702414

TITLE: [Angioscopic evaluation of the immediate result of coronary
angioplasty in relation to balloon inflation time].
Evaluation angioscopique du resultat immediat de
l'angioplastie coronaire en fonction de la duree des
gonflages du ballonnet.

AUTHOR: Eltchaninoff H; Cribier A; Koning R; Jolly N; Baala B;
Farid N; Letac B

CORPORATE SOURCE: Service de cardiologie, hopital Charles-Nicolle, CHU de
Rouen.

SOURCE: Archives des maladies du coeur et des vaisseaux, (1994 Jun)
Vol. 87, No. 6, pp. 721-7.

Journal code: 0406011. ISSN: 0003-9683.

PUB. COUNTRY: France

DOCUMENT TYPE: (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: French

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199505

ENTRY DATE: Entered STN: 10 May 1995

Last Updated on STN: 29 Jan 1996

Entered Medline: 2 May 1995

ABSTRACT:

The aim of this study was to assess the effects of coronary angioplasty on the
intima with respect to the duration of balloon inflation by percutaneous
angioplasty. Twenty-seven patients were randomized according to the total

duration of balloon inflation: Group I "standard" duration (total duration < or = 3 min, N = 13) and Group II: prolonged duration (total duration > or = 12 min, N = 14); the type and distribution of the lesions were comparable in the two groups. The results of angioplasty were evaluated immediately after dilatation by angiography and angioscopy. Angioscopy was performed without failure or complications with perfect definition of the images in all cases. Angioscopy showed 1) intimal tears, 2) thrombi, 3) longitudinal dissections. A classification in three grades was used taking the apparent gravity of the lesions into consideration. The mean duration of balloon inflation in Group I was 205 +/- 45 s and 958 +/- 129 s in Group II. The residual stenosis was 36 +/- 8% in Group I and 26 +/- 10% in Group II (p < 0.05). Angioscopy showed the frequency of intimal tears to be twice greater in Group I (9 cases) than in Group II (4 cases) (p = 0.05). Intravascular thrombi were observed in 13 cases, 6 in Group I and 7 in Group II. One case of longitudinal dissection was observed in each group: only one of these two cases was detected at angiography. The authors conclude that repeated and prolonged balloon inflations improve the immediate results of angioplasty with less residual stenosis at angiography and a lower incidence of intimal tears at angioscopy.

CONTROLLED TERM: Check Tags: Female; Male

Aged

***Angioplasty, Transluminal, Percutaneous Coronary**

***Angioscopy**

***Coronary Disease: TH, therapy**

***Coronary Vessels**

English Abstract

Humans

Image Processing, Computer-Assisted

Middle Aged

Random Allocation

Time Factors

L16 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:182137 BIOSIS

DOCUMENT NUMBER: PREV200600184249

TITLE: Prasugrel (CS-747, LY640315) hydrochloride, a novel thienopyridine prodrug, shows potent antiplatelet and antithrombotic effects with rapid onset of action in rats.

AUTHOR(S): Niitsu, Yoichi [Reprint Author]; Ogawa, Taketoshi; Sugidachi, Atsuhiko; Jakubowski, Joseph A.; Yokouchi, Yuki; Kakusaka, Mayumi; Hasegawa, Michihiro; Asai, Fumitoshi

CORPORATE SOURCE: Sankyo Co Ltd, Pharmacol and Mol Biol Res Labs, Tokyo, Japan

SOURCE: Blood, (NOV 16 2005) Vol. 106, No. 11, Part 1, pp. 534A. Meeting Info.: 47th Annual Meeting of the American-Society-of-Hematology. Atlanta, GA, USA. December 10 -13, 2005. Amer Soc Hematol. CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 15 Mar 2006

Last Updated on STN: 15 Mar 2006

ABSTRACT: The thienopyridine antiplatelet prodrug clopidogrel bisulfate (C) is widely used for atherothrombotic diseases. However, several reports have described a limitation of C, namely poor platelet inhibition in many patients following oral dosing. Prasugrel (hydrochloride): currently under investigation in a Phase 3 trial in acute coronary syndrome patients undergoing percutaneous coronary intervention, is a novel thienopyridine antiplatelet prodrug. In recent clinical studies, prasugrel has

shown more consistent platelet inhibition than C. To date, several preclinical studies have demonstrated that the prasugrel base formulation has more potent antiplatelet and antithrombotic effects than C. The effects of prasugrel hydrochloride (P), which has a higher solubility than the base formulation, have not been reported. The present studies examined the effects of P on platelet aggregation, arterial thrombosis, and bleeding time in rats. Single oral administration of P (0.3 to 3 mg/kg) resulted in inhibition of platelet aggregation (IPA) induced by ADP in a dose- and time-related manner with an ED50 value of 1.1 mg/kg at 4 hr postdose. After dosing of 3 and 10 mg/kg P, statistically significant IPA was observed at 30 and 15 min, and the time required to achieve 50% IPA was approximately 50 and 23 min, respectively (Figure). These results indicate that P has potent antiplatelet effects with an extremely fast onset of action. Multiple P dosing also resulted in potent IPA, with an ED50 value of 0.45 mg/kg/day (p.o.) at 4 hr after the last dose. Our previous report indicated an ED50 value of C at 4 hr after single oral dosing of 16 mg/kg (Br. J. Pharmacol. 129, 1439, 2000), demonstrating about 10-times greater potency of P compared to C. Potent dose-related antithrombotic effects of P were further confirmed in an arterial thrombosis model in rats. P (0.1-1 mg/kg, p.o.) inhibited thrombus formation in the arterial thrombosis induced by extravascular application of FeCl₃ solution. All these results taken together indicate that prasugrel hydrochloride is a novel, potent and fast acting thienopyridine prodrug, potentially providing superior efficacy in the treatment of atherothrombotic disorders.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Blood and hematopoietic agents 22008
Pharmacology - Cardiovascular system 22010
Toxicology - General and methods 22501
Immunology - General and methods 34502

INDEX TERMS: Major Concepts
Pharmacology; Cardiovascular System (Transport and Circulation); Immune System (Chemical Coordination and Homeostasis); Blood and Lymphatics (Transport and Circulation)

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelet: blood and lymphatics

INDEX TERMS: Diseases
arterial thrombosis: vascular disease, drug therapy, chemically-induced
Thrombosis (MeSH)

INDEX TERMS: Chemicals & Biochemicals
ADP; ferric chloride: toxin; clopidogrel bisulfate: anticoagulant-drug, hematologic-drug; prasugrel hydrochloride [CS-747, LY640315]: cardiovascular-drug, antithrombotic-drug, hematologic-drug, anticoagulant-drug, dosage, potency, preclinical trial, efficacy, oral administration

INDEX TERMS: Miscellaneous Descriptors
bleeding time; platelet aggregation inhibition

REGISTRY NUMBER: 175832-20-9 (ADP)
7705-08-0 (ferric chloride)
120202-66-6 (clopidogrel bisulfate)

L16 ANSWER 9 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
 ACCESSION NUMBER: 1996:13245 BIOSIS
 DOCUMENT NUMBER: PREV199698585380
 TITLE: Suppression of intracoronary thrombin activity by weight-adjusted heparin administration during coronary interventions.
 AUTHOR(S): Snitzer, Robert; Hiremath, Yoganand J.; Lee, Joan; Lasala, John M.; Eisenberg, Paul R.; **Winters, Kenneth J.**
 CORPORATE SOURCE: Washington Univ., St. Louis, MO, USA
 SOURCE: Circulation, (1995) Vol. 92, No. 8 SUPPL., pp. I609. Meeting Info.: 68th Scientific Session of the American Heart Association. Anaheim, California, USA. November 13-16, 1995.
 CODEN: CIRCAZ. ISSN: 0009-7322.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 4 Jan 1996
 Last Updated on STN: 4 Jan 1996
 CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
 Biochemistry studies - Proteins, peptides and amino acids 10064
 Biochemistry studies - Carbohydrates 10068
 Enzymes - Physiological studies 10808
 Pathology - Therapy 12512
 Metabolism - Proteins, peptides and amino acids 13012
 Cardiovascular system - Physiology and biochemistry 14504
 Blood - Blood and lymph studies 15002
 Pharmacology - Clinical pharmacology 22005
 Pharmacology - Blood and hematopoietic agents 22008
 INDEX TERMS: Major Concepts
 Blood and Lymphatics (Transport and Circulation);
 Cardiovascular System (Transport and Circulation);
 Enzymology (Biochemistry and Molecular Biophysics);
 Metabolism; Pharmacology
 INDEX TERMS: Chemicals & Biochemicals
 THROMBIN; HEPARIN
 INDEX TERMS: Miscellaneous Descriptors
 ACTIVATED CLOTTING TIME; ANTICOAGULANT-DRUG; DIRECTIONAL CORONARY ATHERECTOMY; HEPARIN; MEETING ABSTRACT;
PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY; THERAPY
 ORGANISM: Classifier
 Hominidae 86215
 Super Taxa
 Primates; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 human
 Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates
 REGISTRY NUMBER: 9002-04-4 (THROMBIN)
 9005-49-6 (HEPARIN)

L16 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
 ACCESSION NUMBER: 1996:13242 BIOSIS
 DOCUMENT NUMBER: PREV199698585377

TITLE: Heparin-resistant thrombin activity is associated with acute ischemic events during high-risk coronary interventions.

AUTHOR(S): Winters, Kenneth J. [Reprint author]; Oltrona, Luigi; Hiremath, Yoganand J. [Reprint author]; Lasala, John M. [Reprint author]; Eisenberg, Paul R. [Reprint author]

CORPORATE SOURCE: Washington Univ., St. Louis, MO, USA

SOURCE: Circulation, (1995) Vol. 92, No. 8 SUPPL., pp. I608. Meeting Info.: 68th Scientific Session of the American Heart Association. Anaheim, California, USA. November 13-16, 1995. CODEN: CIRCAZ. ISSN: 0009-7322.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 4 Jan 1996
Last Updated on STN: 4 Jan 1996

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Enzymes - Physiological studies 10808
Pathology - Therapy 12512
Metabolism - Proteins, peptides and amino acids 13012
Cardiovascular system - Heart pathology 14506
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood and lymph studies 15002
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cardiovascular Medicine (Human Medicine, Medical Sciences); Enzymology (Biochemistry and Molecular Biophysics); Hematology (Human Medicine, Medical Sciences); Metabolism; Pharmacology

INDEX TERMS: Chemicals & Biochemicals
HEPARIN; THROMBIN

INDEX TERMS: Miscellaneous Descriptors
ANTICOAGULANT-DRUG; CORONARY REVASCULARIZATION; HEPARIN; MEETING ABSTRACT; PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY; THROMBOSIS

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

REGISTRY NUMBER: 9005-49-6 (HEPARIN)
9002-04-4 (THROMBIN)

L16 ANSWER 11 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1996:10516 BIOSIS

DOCUMENT NUMBER: PREV199698582651
 TITLE: Thrombin inhibition by novel arginal tripeptide LY296516 fails to inhibit intimal thickening in a rabbit model of arterial injury.
 AUTHOR(S): Dube, Gregory P.; Kurtz, William L.; Brune, Kellie A.; Shuman, Robert T.; **Jakubowski, Joseph A.**; Craft, Trelia J.; Coffman, William J.; Smith, Gerald F.
 CORPORATE SOURCE: Eli Lilly Co., Indianapolis, IN, USA
 SOURCE: Circulation, (1995) Vol. 92, No. 8 SUPPL., pp. I35. Meeting Info.: 68th Scientific Session of the American Heart Association. Anaheim, California, USA. November 13-16, 1995.
 CODEN: CIRCAZ. ISSN: 0009-7322.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 4 Jan 1996
 Last Updated on STN: 4 Jan 1996
 CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
 Cytology - Animal 02506
 Biochemistry studies - Proteins, peptides and amino acids 10064
 Pathology - Therapy 12512
 Cardiovascular system - General and methods 14501
 Cardiovascular system - Blood vessel pathology 14508
 Blood - Blood and lymph studies 15002
 INDEX TERMS: Major Concepts
 Blood and Lymphatics (Transport and Circulation);
 Cardiovascular System (Transport and Circulation)
 INDEX TERMS: Chemicals & Biochemicals
 THROMBIN
 INDEX TERMS: Miscellaneous Descriptors
 MEETING ABSTRACT; **PERCUTANEOUS** TRANSLUMINAL
CORONARY ANGIOPLASTY; RESTENOSIS
 ORGANISM: Classifier
 Leporidae 86040
 Super Taxa
 Lagomorpha; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 Leporidae
 Taxa Notes
 Animals, Chordates, Lagomorphs, Mammals, Nonhuman
 Vertebrates, Nonhuman Mammals, Vertebrates
 REGISTRY NUMBER: 9002-04-4 (THROMBIN)

L16 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1994:202100 BIOSIS
 DOCUMENT NUMBER: PREV199497215100
 TITLE: Adaptation of myocardial ischemia to repetitive prolonged coronary occlusion in PTCA: Clinical, ECG, echocardiographic and metabolic assessment.
 AUTHOR(S): Cribier, Alain; Eltchaninoff, Helene; Tron, Christophe; Koning, Rene; Derumeaux, Genevieve; Baala, Brahim; **Farid, Nasser**; Hecksweiller, Bernadette; Letac, Brice
 CORPORATE SOURCE: Hopital Charles Nicolle, Univ. Rouen, France
 SOURCE: Journal of the American College of Cardiology, (1994) Vol. 0, No. SPEC. ISSUE, pp. 80A.

Meeting Info.: 43rd Annual Scientific Session of the
American College of Cardiology. Atlanta, Georgia, USA.
March 13-17, 1994.

CODEN: JACCDI. ISSN: 0735-1097.

DOCUMENT TYPE:

Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE:

English

ENTRY DATE:

Entered STN: 2 May 1994

Last Updated on STN: 2 May 1994

CONCEPT CODE:

General biology - Symposia, transactions and proceedings
00520

Biochemistry studies - General 10060

Anatomy and Histology - Surgery 11105

Anatomy and Histology - Radiologic anatomy 11106

Pathology - Therapy 12512

Metabolism - General metabolism and metabolic pathways
13002

Cardiovascular system - Heart pathology 14506

Cardiovascular system - Blood vessel pathology 14508

Muscle - Pathology 17506

INDEX TERMS:

Major Concepts

Cardiovascular Medicine (Human Medicine, Medical
Sciences); Metabolism; Morphology; Muscular System
(Movement and Support); Surgery (Medical Sciences)

INDEX TERMS:

Miscellaneous Descriptors

CHRONIC ISCHEMIA; ELECTROCARDIOGRAPHY; MEETING ABSTRACT;
PERCUTANEOUS TRANSLUMINAL CORONARY
ANGIOPLASTY

ORGANISM:

Classifier

Hominidae 86215

Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

human

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates,
Vertebrates

L16 ANSWER 13 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN

ACCESSION NUMBER: 1993:494346 BIOSIS

DOCUMENT NUMBER: PREV199345105571

TITLE: Angioscopic evaluation of the immediate results of PTCA
using prolonged sequential balloon inflations: A comparison
with standard inflations.

AUTHOR(S): Eltchaninoff, H.; Cribier, A.; Koning, R.; Chan, C.; Baala,
C.; Farid, N.; Jolly, N.; Saoudi, N.; Mechmeche,
R.; Letac, B.

CORPORATE SOURCE: Hop C. Nicolle Voacomed, Univ. Rouen, Rouen, France

SOURCE: European Heart Journal, (1993) Vol. 14, No. ABSTR. SUPPL.,
pp. 475.

Meeting Info.: XVth Congress of the European Society of
Cardiology. Nice, France. August 29-September 2, 1993.

CODEN: EHJODF. ISSN: 0195-668X.

DOCUMENT TYPE:

Conference; (Meeting)

LANGUAGE:

English

ENTRY DATE:

Entered STN: 28 Oct 1993

Last Updated on STN: 28 Oct 1993

CONCEPT CODE:

General biology - Symposia, transactions and proceedings
00520

Radiation biology - Radiation and isotope techniques
06504
Biophysics - Methods and techniques 10504
Anatomy and Histology - Surgery 11105
Anatomy and Histology - Radiologic anatomy 11106
Pathology - Therapy 12512
Cardiovascular system - General and methods 14501
Cardiovascular system - Heart pathology 14506
Cardiovascular system - Blood vessel pathology 14508

INDEX TERMS: Major Concepts
Cardiovascular Medicine (Human Medicine, Medical
Sciences); Cardiovascular System (Transport and
Circulation); Radiology (Medical Sciences)

INDEX TERMS: Miscellaneous Descriptors
ABSTRACT; ANALYTICAL METHOD; LUMINAL STENOSIS;
MYOCARDIAL INFARCTION; **PERCUTANEOUS**
TRANSLUMINAL **CORONARY** ANGIOPLASTY

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates,
Vertebrates

=> fil reg; d ide 17
FILE 'REGISTRY' ENTERED AT 11:22:50 ON 10 AUG 2006
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DICTIONARY FILE UPDATES: 9 AUG 2006 HIGHEST RN 900096-56-2

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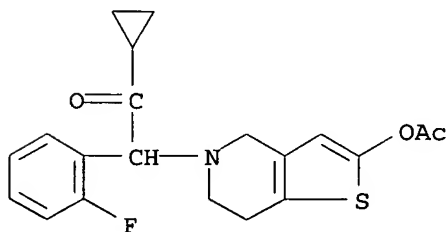
TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 150322-43-3 REGISTRY
ED Entered STN: 29 Sep 1993
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-
cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Thieno[3,2-c]pyridine, ethanone deriv.
OTHER NAMES:
CN CS 747
CN Prasugrel
FS 3D CONCORD
MF C20 H20 F N O3 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, CA, CAPLUS, CIN, IMSDRUGNEWS,
IMSPATENTS, IMSRESEARCH, IPA, PROMT, PROUSDDR, SYNTHLINE, TOXCENTER,
USAN, USPAT2, USPATFULL

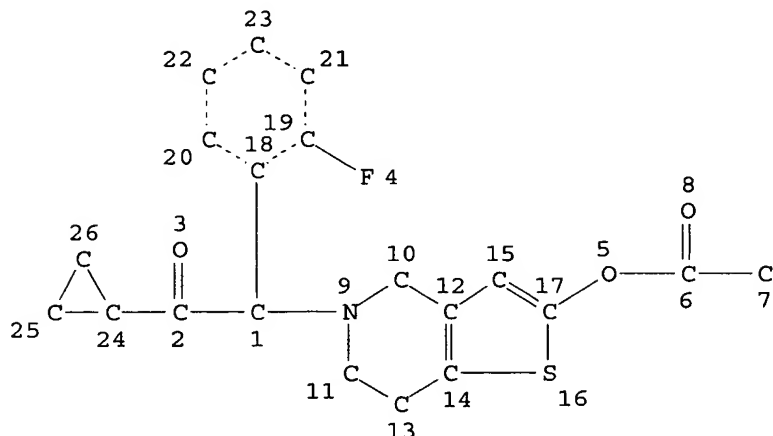


Formula I

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 27 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d stat que l19
 L17 STR



NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 14 ITERATIONS
 SEARCH TIME: 00.00.01

3 ANSWERS

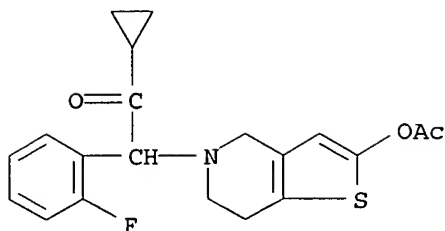
=> d ide l19 1-3; fil capl; d que nos l20; s l20 not 15; fil embase; d que nos l33
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 fil capl; d que nos l20; s l20 not 15; fil embase; d que nos l33

L19 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
 RN 389574-20-3 REGISTRY
 ED Entered STN: 05 Feb 2002
 CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C20 H20 F N O3 S . C4 H4 O4
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

CM 1

CRN 150322-43-3
 CMF C20 H20 F N O3 S

Handwritten note:
 Similar structure to
 an structure of Formula I
 to indicate exact compound, which
 is a benzene, multi-benzene and
 substance, B-3-topically, but still
 forms.

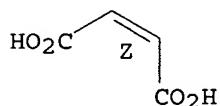


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



4 REFERENCES IN FILE CA (1907 TO DATE)

4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L19 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN

RN 389574-19-0 REGISTRY

ED Entered STN: 05 Feb 2002

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)-, hydrochloride (9CI) (CA INDEX NAME)

OTHER NAMES:

CN LY 640315

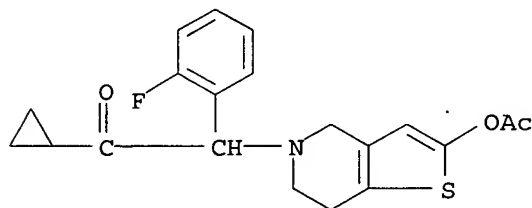
CN Prasugrel hydrochloride

MF C20 H20 F N O3 S . Cl H

SR CA

LC STN Files: ADISINSIGHT, CA, CAPLUS, EMBASE, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

CRN (150322-43-3)

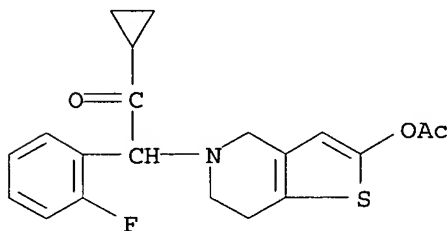
*compound of claim 5*

● HCl

6 REFERENCES IN FILE CA (1907 TO DATE)

6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L19  ANSWER 3 OF 3  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   150322-43-3  REGISTRY
ED   Entered STN:  29 Sep 1993
CN   Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-
      cyclopropyl-2-(2-fluorophenyl)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Thieno[3,2-c]pyridine, ethanone deriv.
OTHER NAMES:
CN   CS 747
CN   Prasugrel
FS   3D CONCORD
MF   C20 H20 F N O3 S
CI   COM
SR   CA
LC   STN Files:  ADISINSIGHT, ADISNEWS, BIOSIS, CA, CAPLUS, CIN, IMSDRUGNEWS,
      IMSPATENTS, IMSRESEARCH, IPA, PROMT, PROUSDDR, SYNTHLINE, TOXCENTER,
      USAN, USPAT2, USPATFULL
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****PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT****

26 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
27 REFERENCES IN FILE CAPLUS (1907 TO DATE)

FILE 'EMBASE' ENTERED AT 11:35:21 ON 10 AUG 2006
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FILE COVERS 1974 TO 10 Aug 2006 (20060810/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L17          STR
L19          3 SEA FILE=REGISTRY FAM FUL L17
L25          34 SEA FILE=EMBASE ABB=ON   L19
L26    1218793 SEA FILE=EMBASE ABB=ON   CARDIOVASCULAR DISEASE+NT/CT
L27    14231 SEA FILE=EMBASE ABB=ON   PCI OR PERCUTANEOUS?(5A)CORONARY
L28    13711 SEA FILE=EMBASE ABB=ON   TRANSLUMINAL CORONARY ANGIOPLASTY/CT

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L30 82369 SEA FILE=EMBASE ABB=ON ACETYLSALICYLIC ACID/CT
L31 27019 SEA FILE=EMBASE ABB=ON STENT+NT/CT
L33 23 SEA FILE=EMBASE ABB=ON L25 AND (L30 OR L31) AND (L26 OR L27
OR L28)

=> fil ipa biosis toxcenter imsre prousddr; d que nos 123

FILE 'IPA' ENTERED AT 11:35:41 ON 10 AUG 2006

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FILE 'TOXCENTER' ENTERED AT 11:35:41 ON 10 AUG 2006

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FILE 'IMSRESEARCH' ENTERED AT 11:35:41 ON 10 AUG 2006

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FILE 'PROUSDDR' ENTERED AT 11:35:41 ON 10 AUG 2006

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L17 STR
L19 3 SEA FILE=REGISTRY FAM FUL L17
L23 27 SEA L19

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FILE LAST UPDATED: 9 AUG 2006 <20060809/UP>
MOST RECENT DERWENT UPDATE: 200651 <200651/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE

http://www.stn-international.de/stndatabases/details/ipc_reform.html and

<http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf> <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS

INDEX ENHANCEMENTS PLEASE VISIT:

http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

L37 11 SEA FILE=WPIX ABB=ON RA7RM2/DCN OR 199852-0-0-0/DCRE OR
PRASUGREL/BI,ABEX OR CS747/BI,ABEX OR CS 747/BI,ABEX
L39 4469 SEA FILE=WPIX ABB=ON R00034/DCN OR R06663/DCN OR 87874-0-0-0/D
CRE OR ASPIRIN/BI,ABEX OR ACETYLSALICYLIC/BI,ABEX OR ACETYL
SALICYLIC/BI,ABEX
L40 8483 SEA FILE=WPIX ABB=ON STENT#/BI,ABEX
L41 4848 SEA FILE=WPIX ABB=ON PCI/BI,ABEX OR (PERCUTANEOUS?/BI,ABEX OR

PER CUTANEOUS?/BI, ABEX OR TRANSLUMINAL?/BI, ABEX OR TRANS
LUMINAL?/BI, ABEX) (5A) CORONARY/BI, ABEX
L42 9 SEA FILE=WPIX ABB=ON L37 AND (L39 OR L40 OR L41)

=> fil capl; d que nos l48; d que nos l51; s l48, l51 not l5
FILE 'CAPLUS' ENTERED AT 11:46:37 ON 10 AUG 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 10 Aug 2006 VOL 145 ISS 7
FILE LAST UPDATED: 9 Aug 2006 (20060809/ED)

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<http://www.cas.org/infopolicy.html>
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L17 STR
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L20 27 SEA FILE=CAPLUS ABB=ON L19
L44 1 SEA FILE=REGISTRY ABB=ON ASPIRIN/CN
L45 20321 SEA FILE=CAPLUS ABB=ON L44
L46 4141 SEA FILE=CAPLUS ABB=ON STENT#/OBI
L47 7059 SEA FILE=CAPLUS ABB=ON (PCI OR (PERCUTANEOUS? OR PER CUTANEOUS
? OR TRANSLUMINAL? OR TRANS LUMINAL?) (5A) CORONARY)/BI
L48 12 SEA FILE=CAPLUS ABB=ON L20 AND (L45 OR L46 OR L47)

L17 STR
L19 3 SEA FILE=REGISTRY FAM FUL L17
L20 27 SEA FILE=CAPLUS ABB=ON L19
L51 1 SEA FILE=CAPLUS ABB=ON L20 AND COATINGS/TI

L52 12 (L48 OR L51) NOT (L5) *Handwritten: 12 (L48 OR L51) NOT (L5) 12 (L48 OR L51) NOT (L5)*

=> dup rem l52, l23, l33, l42
DUPLICATE IS NOT AVAILABLE IN 'IMSRESEARCH, PROUSDDR'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
FILE 'CAPLUS' ENTERED AT 11:47:14 ON 10 AUG 2006
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PROCESSING COMPLETED FOR L52

PROCESSING COMPLETED FOR L23

PROCESSING COMPLETED FOR L33

PROCESSING COMPLETED FOR L42

L53 56 DUP REM L52 L23 L33 L42 (15 DUPLICATES REMOVED)

ANSWERS '1-12' FROM FILE CAPLUS

ANSWERS '13-14' FROM FILE IPA

ANSWERS '15-23' FROM FILE BIOSIS

ANSWERS '24-28' FROM FILE TOXCENTER

ANSWER '29' FROM FILE IMSRESEARCH

ANSWER '30' FROM FILE PROUSDDR

ANSWERS '31-53' FROM FILE EMBASE

ANSWERS '54-56' FROM FILE WPIX

=> d ibib ed abs hitstr 1-12; d iall 13-53; d iall abeq tech 54-56; fil hom

L53 ANSWER 1 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2006:170095 CAPLUS

DOCUMENT NUMBER: 144:226296

TITLE: Oral prophylactic agents for thrombosis and embolism

INVENTOR(S): Morishima, Yoshiyuki; Watanabe, Kengo

PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 29 pp.

CODEN: JKXXAF

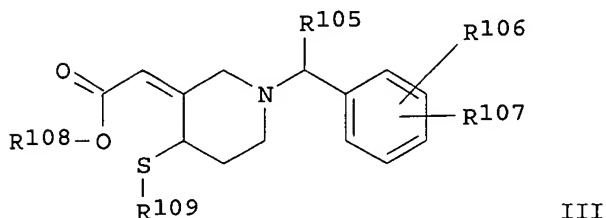
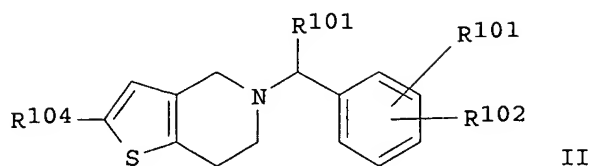
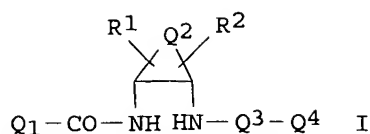
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

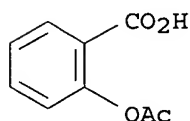
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

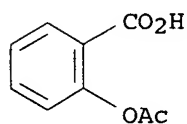
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006052208	A2	20060223	JP 2005-202010	20050711
PRIORITY APPLN. INFO.:			JP 2004-205486	A 20040713
OTHER SOURCE(S):	MARPAT	144:226296		
ED Entered STN:	24 Feb 2006			
GI				



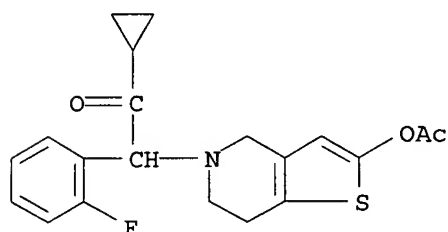
- AB Title agents contain diamines I [Q1 = (un)substituted 4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl, 4,5,6,7-tetrahydrothiazolo[4,5-c]pyridin-2-yl, 4,5,6,7-tetrahydrothieno[2,3-c]pyridin-2-yl, 4,5,6,7-tetrahydrooxazolo[5,4-c]pyridin-2-yl, 4,6-dihydro-5H-pyrrolo[3,4-d]thiazol-2-yl, etc.; Q2 = C1-8 alkylene, (CH₂)_pA(CH₂)_q (p, q = 1-3; p + q = 2-4); A = O, N, S, SO, SO₂, NH; R1, R2 = H, OH, NH₂, CO₂H, (halo)alkyl, acyl, alkoxycarbonylalkyl, (un)substituted acylamino, (un)substituted 3- to 6-membered heterocyclylcarbonyl, etc.; Q3 = CO, SO₂, COCONH, CSCONH, COCSNH, CSCSNH; Q4 = (un)substituted Ph, naphthyl, pyridyl, pyrimidyl, indolyl, benzothienyl, furyl, etc.] and antiplatelet agents chosen from aspirin, sarpogrelate, limaprost, cilostazol, and piperidines II or III [R101, R105 = H, lower alkyl, lower alkoxycarbonyl, lower alkylcarbonyl; R102, R103, R106, R107 = H, lower alkyl, halo; R104 = H, OH, lower alkylcarbonyloxy; R108 = H, lower alkyl; R109 = H, lower alkylcarbonyl] as active ingredients. Thus, combination use of N1-(5-chloropyridin-2-yl)-N2-[(1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-[[5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino]cyclohexyl]ethanediamide HCl salt (IV) and ticlopidine prevented 75% thrombosis formation in rats. CYP2D6- and CYP3A4-dependent metabolism of IV was 0.1-0.81 pmol/pmol/CYP/min, suggesting nonsusceptibility of IV to the enzymes.
- IT 50-78-2, Aspirin 50-78-2D, Aspirin, mixts. containing 150322-43-3 150322-43-3D, mixts. containing
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combination use of diamines and antiplatelet agents for oral prophylactic agents for thrombosis and embolism)
- RN 50-78-2 CAPLUS
- CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



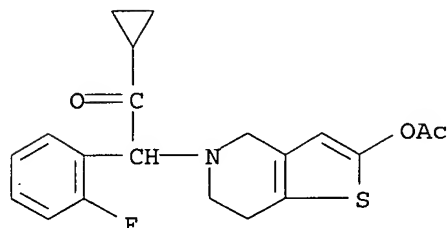
RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L53 ANSWER 2 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2005:902874 CAPLUS
DOCUMENT NUMBER: 143:248277
TITLE: Preparation of sulfonylpyrrolidines as modulators of androgen receptor
INVENTOR(S): Hamann, Lawrence H.; Bi, Yingzhi; Manfredi, Mark C.; Nirschl, Alexandra A.; Sutton, James C.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077925	A1	20050825	WO 2005-US2834	20050202

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

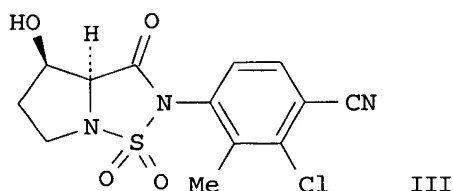
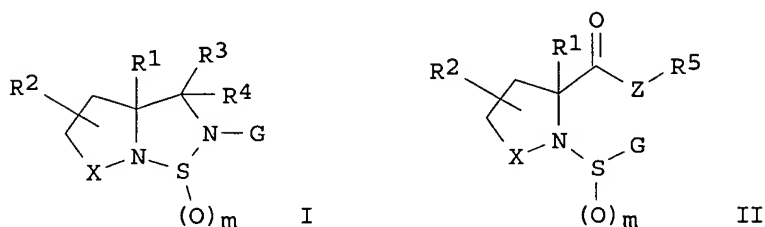
US 2004-541869P

P 20040204

OTHER SOURCE(S): MARPAT 143:248277

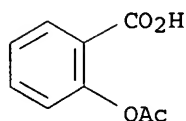
ED Entered STN: 26 Aug 2005

GI

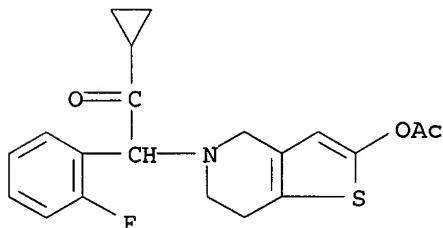


AB Title compds. I or II [R1 = H, (un)substituted alkyl, alkenyl, etc.; R2 = H, halo, SR6, etc.; R3 and R4 independently = H, (un)substituted alkynyl, cycloalkyl, etc.; R5 = H, (un)substituted aryl, arylalkyl, etc.; R6 = H, CHF2, CF3, etc.; X = (CH2)n; G = (un)substituted aryl, heterocycle or heteroaryl; Z = O or NR7; R7 = H, (un)substituted alkyl, alkenyl, etc.; n and m independently = 1-2] and their pharmaceutically acceptable salts, are prepared and disclosed as modulators of androgen receptor. Thus, e.g., III was prepared by hydrolysis of (2S,3R)-1-(3-chloro-4-cyano-2-methylphenylsulfamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid Me ester (preparation given) followed by cyclization. The activity of I was evaluated in transactivation assays of a transfected reporter construct and using the endogenous androgen receptor of the host cells (no data). I as modulator of androgen receptor should prove useful in the treatment of neoplasm, Alzheimer's disease and obesity. Pharmaceutical compns. comprising I are disclosed.

IT 50-78-2, Aspirin 150322-43-3, CS-747
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drug; preparation of sulfonylpyrrolidines as modulators of
androgen receptor)
RN 50-78-2 CAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 3 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2005:961492 CAPLUS
DOCUMENT NUMBER: 143:254076
TITLE: Drug eluting coatings for medical implants
and methods of use
INVENTOR(S): Hsu, Li-Chien
PATENT ASSIGNEE(S): Bioteegra, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U.S.
Ser. No. 423,718.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

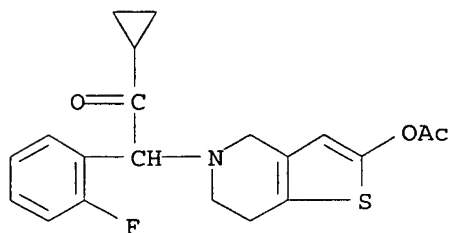
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005191333	A1	20050901	US 2005-119075	20050428
US 2004037886	A1	20040226	US 2003-423718	20030426
PRIORITY APPLN. INFO.:			US 2002-405933P	P 20020826
			US 2003-423718	A2 20030426

ED Entered STN: 02 Sep 2005
AB A drug coating for a medical device comprises one or more drug composite layers. The drug composite layer comprises one or more therapeutic agents dispersed within one or more modified bioactive binders. The modified bioactive binders are hydrophobic compds. bonded to bioactive binders, and the modified bioactive binders are not inert polymers.
IT 150322-43-3, Prasugrel

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug eluting coatings for medical implants and methods of use)

RN 150322-43-3 CAPLUS

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L53 ANSWER 4 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2005:904349 CAPLUS

DOCUMENT NUMBER: 143:248278

TITLE: Preparation of sulfonylpyrrolidines as modulators of androgen receptor

INVENTOR(S): Hamann, Lawrence G.; Bi, Yingzhi; Manfredi, Mark C.; Nirschl, Alexandra A.; Sutton, James C.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 35 pp.

CODEN: USXXCO

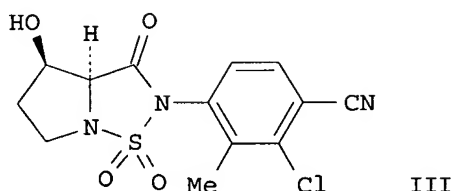
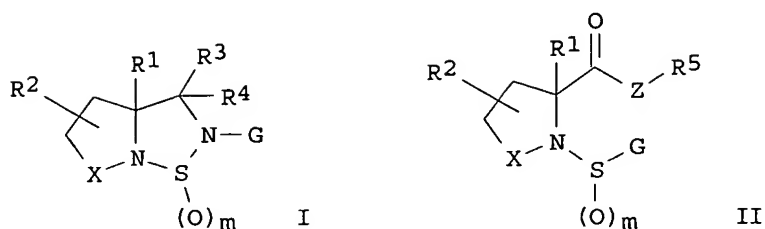
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005187267	A1	20050825	US 2005-48439	20050201
PRIORITY APPLN. INFO.:			US 2004-541869P	P 20040204
OTHER SOURCE(S):	MARPAT	143:248278		
ED Entered STN:		26 Aug 2005		
GI				



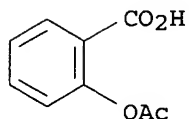
AB Title compds. I or II [R1 = H, (un)substituted alkyl, alkenyl, etc.; R2 = H, halo, SR6, etc.; R3 and R4 independently = H, (un)substituted alkynyl, cycloalkyl, etc.; R5 = H, (un)substituted aryl, arylalkyl, etc.; R6 = H, CHF2, CF3, etc.; X = (CH2)n; G = (un)substituted aryl, heterocycle or heteroaryl; Z = O or NR7; R7 = H, (un)substituted alkyl, alkenyl, etc.; n and m independently = 1-2] and their pharmaceutically acceptable salts, are prepared and disclosed as modulators of androgen receptor. Thus, e.g., III was prepared by hydrolysis of (2S,3R)-1-(3-chloro-4-cyano-2-methyl-phenylsulfamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid Me ester (preparation given) followed by cyclization. The activity of I was evaluated in transactivation assays of a transfected reporter construct and using the endogenous androgen receptor of the host cells (no data). I as modulator of androgen receptor should prove useful in the treatment of neoplasm, Alzheimer's disease and obesity. Pharmaceutical compns. comprising I are disclosed.

IT 50-78-2 150322-43-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drug; preparation of sulfonylpyrrolidines as modulators of androgen receptor)

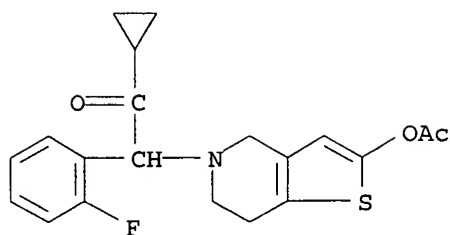
RN 50-78-2 CAPLUS

CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



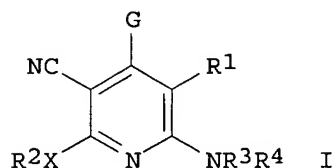
RN 150322-43-3 CAPLUS

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L53 ANSWER 5 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
 ACCESSION NUMBER: 2005:824492 CAPLUS
 DOCUMENT NUMBER: 143:222525
 TITLE: Method of using 3-cyano-4-arylpyridine derivatives as modulators of androgen receptor function, preparation thereof, and use with other agents
 INVENTOR(S): Nirschl, Alexandra A.; Hamann, Lawrence G.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 25 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005182105	A1	20050818	US 2005-48437	20050201
PRIORITY APPLN. INFO.:			US 2004-541780P	P 20040204
OTHER SOURCE(S): MARPAT 143:222525				
ED Entered STN: 19 Aug 2005				
GI				



AB A method is provided for treating androgen receptor-associated conditions, such as age-related diseases, e.g. sarcopenia, employing a compound I [R1 = CN, H; X = O, S; R2 = (substituted) alkyl, (substituted) cycloalkyl, etc; R3, R4 = H, (substituted) alkyl, etc.; G = (substituted) aryl, (substituted) heteroaryl], or a pharmaceutically acceptable salt or prodrug ester thereof. Preparation of selected I is described. I may be used in combination with other agents.

IT 50-78-2, Aspirin 150322-43-3, CS-747
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyanoarylpyridine derivative modulators of androgen receptor function, preparation, and use with other agents)

RN 50-78-2 CAPLUS
 CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)

(TIMI major plus minor) non-CABG-related bleeding events in prasugrel- vs. clopidogrel-treated patients. Hemorrhagic complications were infrequent, with no significant difference between patients treated with prasugrel or clopidogrel in the rate of significant bleeding (1.7% vs. 1.2%; hazard ratio, 1.42; 95% CI, 0.40, 5.08). In prasugrel-treated patients, there were numerically lower incidences of the primary efficacy composite end point (30-day major adverse cardiac events) and of the secondary end points myocardial infarction, recurrent ischemia, and clin. target vessel thrombosis. Conclusions: In this phase 2 study, which was designed to assess safety when administered at the time of **percutaneous coronary** intervention, prasugrel and clopidogrel both resulted in low rates of bleeding. The results of this trial serve as a foundation for the large phase 3 clin. trial designed to assess both efficacy and safety.

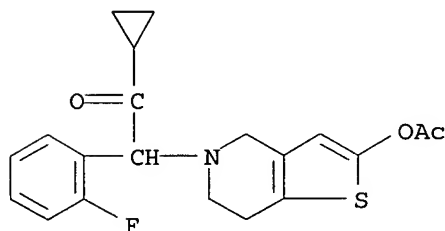
IT 150322-43-3, Prasugrel

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(LY640315; prasugrel and clopidogrel both were safe, effective and resulted in low rates of bleeding in patient after **percutaneous coronary** intervention)

RN 150322-43-3 CAPLUS

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 7 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 2005:480490 CAPLUS

DOCUMENT NUMBER: 143:205548

TITLE: Pharmacology of CS-747 (prasugrel, LY640315), a novel, potent antiplatelet agent with in vivo P2Y12 receptor antagonist activity

AUTHOR(S): Niitsu, Yoichi; Jakubowski, Joseph A.; Sugidachi, Atsuhiko; Asai, Fumitoshi

CORPORATE SOURCE: Pharmacology and Molecular Biology Research Laboratories, Sankyo Co., Ltd., Tokyo, Japan

SOURCE: Seminars in Thrombosis and Hemostasis (2005), 31(2), 184-194

CODEN: STHMBV; ISSN: 0094-6176

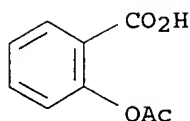
PUBLISHER: Thieme Medical Publishers, Inc.

DOCUMENT TYPE: Journal; General Review

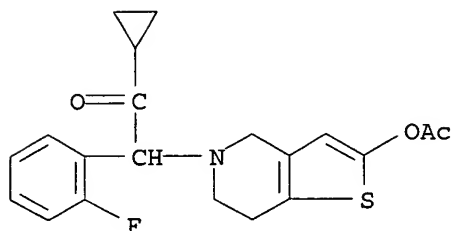
LANGUAGE: English

ED Entered STN: 07 Jun 2005

AB A review. CS-747 (prasugrel, LY640315) is a member of the thienopyridine class of oral platelet aggregation inhibitors that includes ticlopidine and clopidogrel. A single oral administration of CS-747 produced a dose-related inhibition of platelet aggregation in rats that was approx. 10- and 100-fold more potent than that of clopidogrel and ticlopidine,



RN 150322-43-3 CAPLUS
CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L53 ANSWER 6 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2005:548016 CAPLUS

DOCUMENT NUMBER: 143:359712

TITLE: Randomized Comparison of Prasugrel (CS-747, LY640315), a Novel Thienopyridine P2Y₁₂ Antagonist, with Clopidogrel in **Percutaneous Coronary Intervention**

AUTHOR(S): Wiviott, Stephen D.; Antman, Elliott M.; Winters, Kenneth J.; Weerakkody, Govinda; Murphy, Sabina A.; Behounek, Bruce D.; Carney, Robert J.; Lazzam, Charles; McKay, Raymond G.; McCabe, Carolyn H.; Braunwald, Eugene

CORPORATE SOURCE: the JUMBO-TIMI 26 Investigators, TIMI Study Group, Cardiovascular Division, Brigham and Women's Hospital, Department of Medicine, Harvard Medical School, Boston, MA, 02115, USA

SOURCE: Circulation (2005), 111(25), 3366-3373

CODEN: CIRCAZ; ISSN: 0009-7322

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

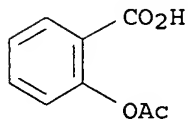
LANGUAGE: English

ED Entered STN: 24 Jun 2005

AB Background: Despite the current standard antiplatelet regimen of aspirin and clopidogrel (with or without glycoprotein IIb/IIIa inhibitors) in **percutaneous coronary** intervention patients, periprocedural and postprocedural ischemic events continue to occur. Prasugrel (CS-747, LY640315), a novel potent thienopyridine P2Y₁₂ receptor antagonist, has the potential to achieve higher levels of inhibition of ADP-induced platelet aggregation than currently approved doses of clopidogrel. Methods and Results: Joint Utilization of Medications to Block Platelets Optimally-Thrombolysis In Myocardial Infarction 26 (JUMBO-TIMI 26) was a phase 2, randomized, dose-ranging, double-blind safety trial of prasugrel vs. clopidogrel in 904 patients undergoing elective or urgent **percutaneous coronary** intervention. Patients were randomized to either standard dosing with clopidogrel or 1 of 3 prasugrel regimens. Subjects were monitored for 30 days for bleeding and clin. events. The primary end point of the trial was clin. significant

L53 ANSWER 8 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 9
 ACCESSION NUMBER: 2002:813926 CAPLUS
 DOCUMENT NUMBER: 137:304829
 TITLE: Enantiomers of N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-4-(2-oxazolyl)[1,1'-biphenyl]-2-yl]methyl]-N,3,3-trimethylbutanamide
 INVENTOR(S): Hughes, David E.; Seidenberg, Beth C.
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 24 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083130	A1	20021024	WO 2002-US11992	20020412
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003040534	A1	20030227	US 2002-121520	20020412
PRIORITY APPLN. INFO.:			US 2001-284080P	P 20010416
ED Entered STN: 25 Oct 2002				
AB Endothelin antagonist N-[[2'-[[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-4-(2-oxazolyl)[1,1'-biphenyl]-2-yl]methyl]-N,3,3-trimethylbutanamide surprisingly exists as separable enantiomeric atropisomers. The (+)-dextrorotatory atropisomer demonstrates remarkably higher potency than either the (-)-levorotatory atropisomer or the racemate. The (+)-dextrorotatory atropisomer is suitable for treatment of endothelin-related disorders, such as hypertension, renal diseases, atherosclerosis, restenosis, congestive heart failure, diabetic nephropathy, cancer, asthma, etc., alone or in combination with, e.g., angiotensin, renin, or ACE inhibitors, diuretics, cardiac glycosides, antiplatelet agents, etc.				
IT 50-78-2, Aspirin 150322-43-3, CS 747				
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combination with; therapeutic uses of enantiomers of biphenyl isoxazole sulfonamide derivative as endothelin antagonists)				
RN 50-78-2 CAPLUS				
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)				



RN 150322-43-3 CAPLUS
 CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)

resp. The antiaggregatory effect of CS-747 was evident at 30 min and lasted until 72 h after dosing, indicating fast onset and long duration of action. CS-747 showed more potent antithrombotic activity compared with clopidogrel and ticlopidine with the same rank order as the antiaggregatory potencies. Combined administration of CS-747 with aspirin to rats produced substantially greater inhibition of both platelet aggregation and thrombus formation compared with each agent alone. The antiplatelet action of CS-747 is due to irreversible and selective blockade of platelet P2Y₁₂ ADP (ADP) receptors by its active metabolite R-138727. In phase I studies, a single oral dose of CS-747 (30 and 75 mg) produced > 50% inhibition of ADP-induced platelet aggregation, with rapid onset (1 h) and long duration (>48 h) of action. In healthy volunteers, once-daily administration of 10 mg CS-747 for 10 days showed significant cumulative inhibition of platelet aggregation from 2 days after the first dose until at least 2 days after the final dose. Studies conducted to date indicate that CS-747 is a highly effective antiplatelet and antithrombotic agent and is anticipated to be effective in the treatment of atherothrombotic and other ischemic vascular diseases.

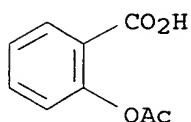
IT 50-78-2, Aspirin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(CS-747 alone or in combination with aspirin exhibited more potent antiplatelet activity and antithrombotic activity than ticlopidine and clopidogrel indicating that CS-747 may be effective in treatment of atherothrombotic disease patient)

RN 50-78-2 CAPLUS

CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



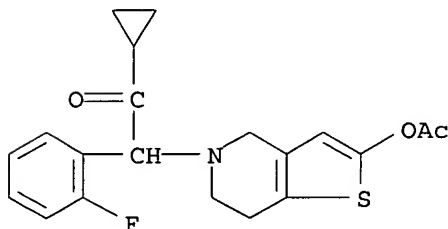
IT 150322-43-3, CS 747

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(LY640315 alone or with aspirin exhibited more potent antiplatelet activity and antithrombotic activity than ticlopidine and clopidogrel indicating that CS-747 may be effective in treatment of patient with atherothrombotic disease)

RN 150322-43-3 CAPLUS

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

46

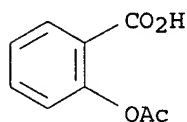
THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(medicinal compns. containing aspirin and thienopyridinylethanone
derivative)

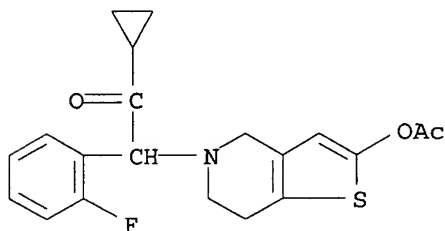
RN 50-78-2 CAPLUS

CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



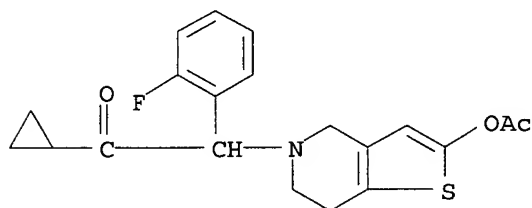
RN 150322-43-3 CAPLUS

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 389574-19-0 CAPLUS

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

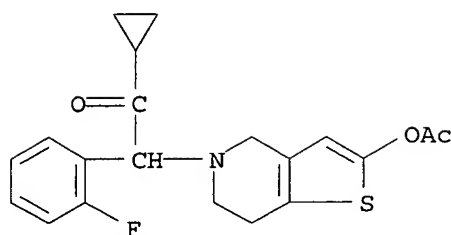
RN 389574-20-3 CAPLUS

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 150322-43-3

CMF C20 H20 F N O3 S



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 9 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 2002:504621 CAPLUS

DOCUMENT NUMBER: 137:52422

TITLE: Medicinal compositions containing aspirin

INVENTOR(S): Asai, Fumitoshi; Sugidachi, Atsuhiko; Ogawa, Taketoshi; Inoue, Teruhiko

PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan; Ube Industries, Ltd.

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002051412	A1	20020704	WO 2001-JP11201	20011220
W: AU, BR, CA, CN, CO, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PH, PL, RU, SG, SK, US, VN, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2432644	AA	20020704	CA 2001-2432644	20011220
JP 2002255814	A2	20020911	JP 2001-386850	20011220
EP 1350511	A1	20031008	EP 2001-271850	20011220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
BR 2001016531	A	20040225	BR 2001-16531	20011220
CN 1491109	A	20040421	CN 2001-822768	20011220
NZ 526540	A	20041126	NZ 2001-526540	20011220
RU 2262933	C2	20051027	RU 2003-118638	20011220
US 2004024013	A1	20040205	US 2003-600266	20030620
ZA 2003004878	A	20040810	ZA 2003-4878	20030623
NO 2003002902	A	20030624	NO 2003-2902	20030624
PRIORITY APPLN. INFO.:			JP 2000-392983	A 20001225
			WO 2001-JP11201	W 20011220

ED Entered STN: 05 Jul 2002

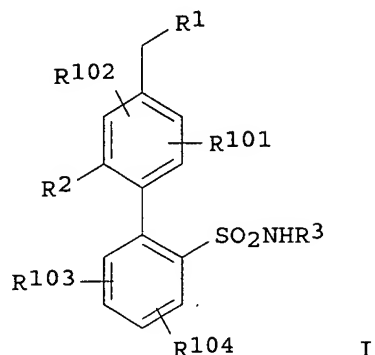
AB Disclosed are medicinal compns. containing as the active ingredients 2-acetoxy-5-(α -cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2 c]pyridine (I) or its pharmacol. acceptable salt and aspirin. Because of having excellent inhibitory effects on platelet aggregation and thrombosis, these compns. are useful as preventives or remedies for diseases induced by thrombus or embolization. A tablet was formulated containing I 10, aspirin 12.5, lactose 175.5, starch 50, and Mg stearate 2 mg.

IT 50-78-2, Aspirin 150322-43-3 389574-19-0
389574-20-3

US 2000-737201

A3 20001214

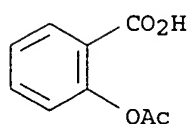
OTHER SOURCE(S): MARPAT 137:263024
 ED Entered STN: 04 Oct 2002
 GI



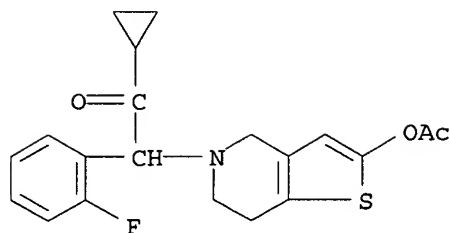
AB Title compds. (I; R1 = specified oxoimidazolyl, pyridoimidazolyl, pyridylamino, pyridyloxy, triazolyl, quinolinyloxy, etc.; R2 = H, halo, CHO, (halo)alkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxy, cyano, OH, NO2, etc.; R3 = heteroaryl; R101-R104 = H, halo, CHO, alkyl, haloalkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkoxyalkyl, alkoxy, alkoxyalkoxy, cyano, OH, hydroxyalkyl, NO2, etc; with provisos) were prepared as dual angiotensin II and endothelin receptor antagonists for treatment of hypertension and other diseases (no data). Thus, 4-BrC6H4CH2OH was coupled with [2-[(4,5-dimethyl-3-isoxazolyl)][2-methoxyethoxy)methyl]amino]sulfonyl]phenyl]boronic acid to give N-(4,5-dimethyl-3-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl][1,1'-biphenyl]-2-sulfonamide (66%). This was brominated to give the 4'-bromomethyl derivative (90%), reacted with 2-butyl-1,3-diazaspiro[4.4]non-1-en-4-one hydrochloride, and deprotected (49% for two steps) to give 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-[1,1'-biphenyl]-2-sulfonamide.

IT 50-78-2, Aspirin 150322-43-3, Cs-747
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

RN 50-78-2 CAPLUS
 CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS
 CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)

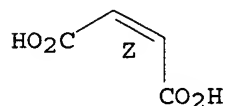


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 10 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 2002:755214 CAPLUS

DOCUMENT NUMBER: 137:263024

TITLE: Preparation of N-isoxazolyl biphenylsulfonamides and related compounds as dual angiotensin II and endothelin receptor antagonists.

INVENTOR(S): Murugesan, Natesan; Tellew, John E.; Macor, Jhon E.; Gu, Zhengxiang

PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA

SOURCE: U.S. Pat. Appl. Publ., 206 pp., Cont.-in-part of U.S. Ser. No. 643,640, abandoned.
CODEN: USXXCO

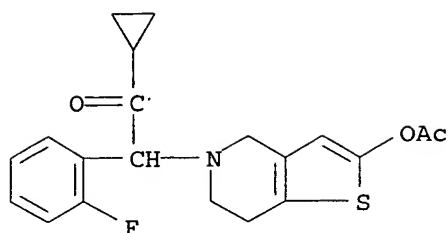
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002143024	A1	20021003	US 2000-737201	20001214
US 6638937	B2	20031028		
US 2004106833	A1	20040603	US 2003-673100	20030926
US 6835741	B2	20041228		
US 2004127515	A1	20040701	US 2003-672572	20030926
US 6852745	B2	20050208		
PRIORITY APPLN. INFO.:			US 1998-91847P	P 19980706
			US 1999-345392	B2 19990701
			US 1999-464037	B2 19991215
			US 2000-481197	B2 20000111
			US 2000-513779	A2 20000225
			US 2000-604322	A2 20000626
			US 2000-643640	B2 20000822



L53 ANSWER 11 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 2001:283949 CAPLUS

DOCUMENT NUMBER: 134:311218

TITLE: Synthesis and use of heterocyclic sodium/proton exchange inhibitors

INVENTOR(S): Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven V.; Ngu, Khehyong; Atwal, Karnail S.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 221 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027107	A2	20010419	WO 2000-US27461	20001002
WO 2001027107	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6887870	B1	20050503	US 2000-669298	20000925
CA 2388813	AA	20010419	CA 2000-2388813	20001002
EP 1224183	A2	20020724	EP 2000-968723	20001002
EP 1224183	B1	20051228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
BR 2000014725	A	20030617	BR 2000-14725	20001002
JP 2003527331	T2	20030916	JP 2001-530325	20001002
NZ 517668	A	20040924	NZ 2000-517668	20001002
AT 314364	E	20060115	AT 2000-968723	20001002
ES 2254236	T3	20060616	ES 2000-968723	20001002
ZA 2002002479	A	20040727	ZA 2002-2479	20020327
NO 2002001717	A	20020610	NO 2002-1717	20020411
US 2005137216	A1	20050623	US 2005-46993	20050131

PRIORITY APPLN. INFO.:

US 1999-158755P P 19991012

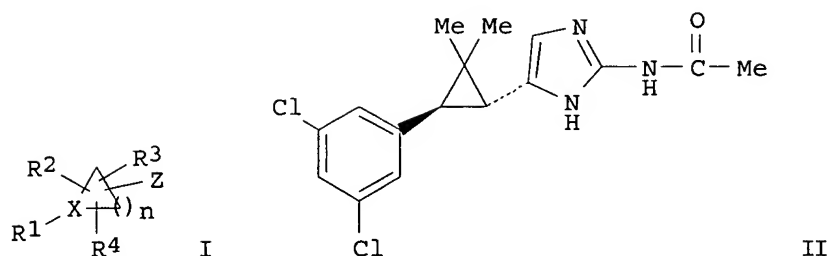
US 2000-669298 A3 20000925

WO 2000-US27461 W 20001002

OTHER SOURCE(S): MARPAT 134:311218

ED Entered STN: 20 Apr 2001

GI



AB Compds. of formula I [wherein; n is 1-5; X is N or CR₅, where R₅ is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R₁ is H, alk(en)(yn)yl, alk(enyl)(ynyl)oxy, (aryl or alkyl)₃Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloheteroaryl, etc.; R₂, R₃ and R₄ are any of the groups set out for R₁ and optionally substituted with 1 to 5 substituents which may be the same or different and when X is N, R₁ is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butyldiethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding α-chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical combinations are claimed using I and certain antihypertensive agents, β-adrenergic agonists, hypolipidemic agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia.

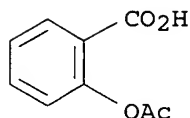
IT 50-78-2, Aspirin 150322-43-3, CS 747

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceuticals also containing; synthesis and use of heterocyclic sodium/proton exchange inhibitors)

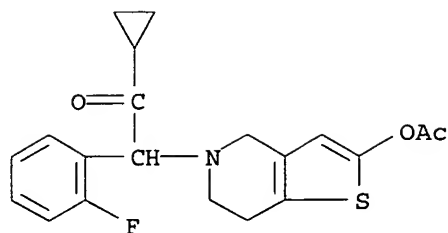
RN 50-78-2 CAPLUS

CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L53 ANSWER 12 OF 56 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1200967 CAPLUS

DOCUMENT NUMBER: 143:460154

TITLE: Preparation of fused heterocyclic compounds as potassium channel modulators

INVENTOR(S): Johnson, James A.; Lloyd, John; Kover, Alexander

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

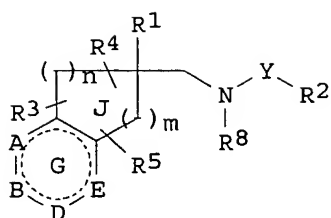
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005105096	A2	20051110	WO 2005-US12542	20050414
WO 2005105096	A3	20060706		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005250783	A1	20051110	US 2005-104856	20050413
PRIORITY APPLN. INFO.:			US 2004-563143P	P 20040415

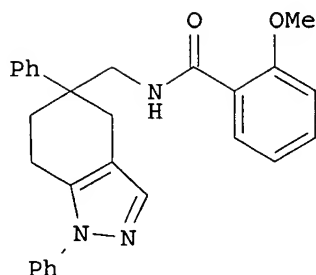
OTHER SOURCE(S): MARPAT 143:460154

ED Entered STN: 11 Nov 2005

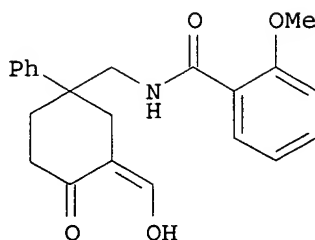
GI



I



II



III

AB Compds. of formula I [n and m are integers such that ring J is a 5-7 membered ring; A, B, D, and E are -CR6=, -CR6-, -CO-, -NR7-, -N=, -O-, -S-, a bond or a double bond, such that ring G is a 5-6 membered heterocycle with at least one N atom; R1 = aryl substituted with one or more X; X = -(CH2)p(Z1)q(CH2)aZ2 which substituents may together form an (un)substituted carbocycle or heterocycle; R2 = aryl, heteroaryl, cycloalkyl or heterocyclo each optionally substituted with one or more X; Y = -CO-, -C(=S)-, -SO2, etc.; R3-8 are the same or different and independently equal to X, or R3-5 may in pairs of two form an (un)substituted carbocycle or heterocycle, or R6 and R7 together in pairs of two form an (un)substituted carbocycle or heterocycle, etc.; Z1 = S, SO, CO, etc.; Z2 = H, (un)substituted alkyl, alkenyl, etc.; p and a independently = 0-10; q = 0-1], and their pharmaceutically acceptable salts, are prepared and disclosed as potassium channel modulators (no data). Thus, e.g., II was prepared by cyclocondensation of III (preparation given)

with

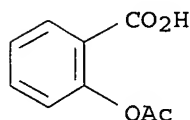
Ph hydrazine. Pharmaceutical compns. are provided.

IT 50-78-2, Aspirin 150322-43-3, CS-747

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fused heterocyclic compds. and their use for treatment of diseases)

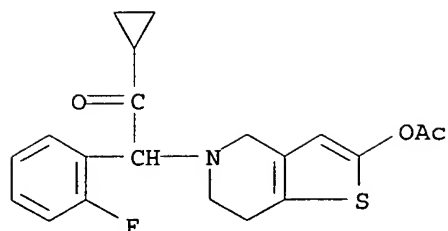
RN 50-78-2 CAPLUS

CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 150322-43-3 CAPLUS

CN Ethanone, 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclopropyl-2-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L53 ANSWER 13 OF 56 IPA COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 2

ACCESSION NUMBER: 2006:8292 IPA
DOCUMENT NUMBER: 43-09792
TITLE: The platelet inhibitory effects and pharmacokinetics of prasugrel after administration of loading and maintenance doses in healthy subjects
AUTHOR: Jakubowski, JA; Payne, CD; Brandt, JT; Weerakkody, GJ; Winters, KJ; et al
CORPORATE SOURCE: Eli Lilly & Co, Lilly Corp Ctr, 6075, Indianapolis, IN 46285, USA joseph@lilly.com
SOURCE: Journal of Cardiovascular Pharmacology (USA), (2006) Vol. 47, pp. 377-384. 30 Refs.
CODEN: JCPCDT; ISSN: 0160-2446.
DOCUMENT TYPE: Journal
FILE SEGMENT: HUMAN
LANGUAGE: English
ABSTRACT:

The results of a double-blind, placebo-controlled, randomized, parallel group study evaluating the platelet inhibitory effects and pharmacokinetics of prasugrel (CS-747) after administration of loading and maintenance doses in healthy subjects (n=28) are presented.

The results from this combined loading dose and maintenance dose study in healthy subjects indicate that prasugrel provides rapid and consistent inhibition of adenosine diphosphate-stimulated platelet aggregation and is well tolerated at the doses and time intervals studied.

SECTION: 15 Drug Metabolism and Body Distribution; 4 Toxicity; 6 Drug Evaluations

CLASSIFICATION: 20:12.04 Platelet aggregation inhibitors

INDEX TERM: CS-747; pharmacokinetics

INDEX TERM: Platelet aggregation; cs-747

INDEX TERM: Pharmacokinetics; cs-747

INDEX TERM: Bleeding time; cs-747

INDEX TERM: Blood levels; cs-747

INDEX TERM: Metabolism; cs-747

INDEX TERM: Toxicity; cs-747

INDEX TERM: Platelet aggregation inhibitors; cs-747

INDEX TERM: Drugs; new

INDEX TERM: Drug administration routes; oral

CAS REGISTRY NO.: 150322-43-3 (CS-747)

CHEMICAL NAME: CS-747 (LY-640315); CS-747 (Prasugrel)

L53 ANSWER 14 OF 56 IPA COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:3127 IPA

DOCUMENT NUMBER: 39-03127
TITLE: CS-747 and R-99224
AUTHOR: Doggrell, S. A.; Mealy, N. E.; Castaner, J.
CORPORATE SOURCE: Reprints: Prous Sci., P.O. Box 540, 08080 Barcelona, Spain
SOURCE: Drugs of the Future (Spain), (Sep 2001) Vol. 26, pp. 835-840. 13 Refs.
CODEN: DRFUD4; ISSN: 0377-8282.

DOCUMENT TYPE: Journal
FILE SEGMENT: HUMAN
LANGUAGE: English
ABSTRACT:

An overview of CS-747 and its active metabolite R-99224, platelet aggregation inhibitors to prevent blood clotting in the coronary artery, is presented, including the synthesis, pharmacological actions, pharmacokinetics, metabolism, and clinical studies.

Elvira deC. Weiss

SECTION: 5 Investigational Drugs; 11 Pharmacology; 15 Drug Metabolism and Body Distribution

CLASSIFICATION: 20:12.04 Platelet aggregation inhibitors; 20:12.04 Platelet aggregation inhibitors

INDEX TERM: CS-747; overview
INDEX TERM: R-99224; metabolites; CS-747
INDEX TERM: Mechanism of action; CS-747; overview
INDEX TERM: Pharmacokinetics; CS-747; overview
INDEX TERM: Metabolism; CS-747; overview
INDEX TERM: Clinical studies; CS-747; overview
INDEX TERM: Platelet aggregation inhibitors; CS-747; overview
INDEX TERM: Platelet aggregation inhibitors; R-99224; overview
CAS REGISTRY NO.: 150322-43-3 (CS-747)
CAS REGISTRY NO.: 239466-75-2 (R-99224)

L53 ANSWER 15 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:34344 BIOSIS
DOCUMENT NUMBER: PREV200600041967
TITLE: Stereoselective inhibition of human platelet aggregation by R-138727, the active metabolite of CS-747 (Prasugrel, LY640315), a novel P2Y(12) receptor inhibitor.
AUTHOR(S): Hasegawa, Michihiro; Sugidachi, Atsuhiko; Ogawa, Taketoshi; Isobe, Takashi; Jakubowski, Joseph A.; Asai, Fumitoshi [Reprint Author]
CORPORATE SOURCE: Sankyo Co Ltd, Pharmacol and Mol Biol Labs, Shinagawa Ku, 1-2-58 Hiromachi, Tokyo 1408710, Japan
toasai@sankyo.co.jp
SOURCE: Thrombosis and Haemostasis, (SEP 2005) Vol. 94, No. 3, pp. 593-598.
CODEN: THHADQ. ISSN: 0340-6245.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Dec 2005
Last Updated on STN: 28 Dec 2005

ABSTRACT: CS-747 (Prasugrel, LY640315) is a thienopyridine antiplatelet prodrug that is metabolized to the thiol-containing active metabolite R-138727, which binds to and irreversibly inhibits the platelet P2Y(12) ADP receptor. R-138727 is composed of 4 stereo-isomers, (R, S)-, (R, R)-, (S, S)-, and (S, R)-isomers (the first letter for the configuration of a chiral center at the sulfur-bearing position and the second for that at the benzylic position). In the present study, we determined the stereoselectivity of P2Y(12) antagonist effects by assessing the antagonism of the [H-3]-2-MeS-ADP that binds to human P2Y(12) receptors expressed in Chinese hamster ovary cells as an affinity

assay, and by the inhibition of ADP-induced aggregation of washed human platelets as a functional assay. R-138727 and its 2 components, R-99224, a mixture of (R, S)- and (S, R)-isomers and R-100364, a mixture of (R, R) and (S, S)-isomers, inhibited [3H]-2-MeS-ADP binding and platelet aggregation. The rank order of potency of these compounds were identical in both assays: R-99224 > R-138727 >> R-100364. Inhibition of ADP-induced platelet aggregation by R-138727 and R-99224 was concentration- and time-related. In experiments using the 4 single stereo-isomers, all isomers inhibited ADP-induced platelet aggregation, but the (R, S)-isomer was found to be the most potent, followed by the (R, R)-isomer. These in vitro studies indicate that R-138727 is an effective antagonist of P2Y₁₂, and potent inhibitor of ADP-induced platelet aggregation, and that these antiplatelet activities of R-138727 are largely dependent on its (R, S)-isomer. This suggests that the (R) configuration of the reactive thiol group of the active metabolite of CS-747 is critical for P2Y₁₂ and platelet inhibitory activities.

CONCEPT CODE: Cytology - Animal 02506
Cytology - Human 02508
Clinical biochemistry - General methods and applications 10006
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008

INDEX TERMS: Major Concepts
Pharmacology; Clinical Chemistry (Allied Medical Sciences); Blood and Lymphatics (Transport and Circulation)

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelet: blood and lymphatics

INDEX TERMS: Chemicals & Biochemicals
ADP; thiol; sulfur; P2Y₁₂ receptor; platelet P2Y₁₂-ADP receptor; (R,S)-isomer; (R,R)-isomer; [tritiated]-2-MeS-ADP; CS-747 [LY640315, Prasugrel]; hematologic-drug; R-138727: hematologic-drug

INDEX TERMS: Miscellaneous Descriptors
stereoselective inhibition

ORGANISM: Classifier
Cricetidae 86310
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
CHO cell line (cell_line): Chinese hamster ovary cells
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

REGISTRY NUMBER: 175832-20-9 (ADP)

7704-34-9 (sulfur)
150322-43-3 (CS-747)
150322-43-3 (LY640315)
150322-43-3 (Prasugrel)

L53 ANSWER 16 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN

ACCESSION NUMBER: 2005:191105 BIOSIS
DOCUMENT NUMBER: PREV200500192971
TITLE: Identification of the cytochromes P450 responsible for the
formation of R-138727, the active metabolite of a novel
thienopyridine anti-platelet agent, CS-747 (LY640315).
AUTHOR(S): Fayer, Jessica L. [Reprint Author]; Eckstein, James A.;
Kasper, Steve C.; Farid, Nagy A.; Wrighton, Steven A.;
Kurihara, Atsushi; Ring, Barbara J.
CORPORATE SOURCE: Lilly Res Labs Div Drug Disposit, Eli Lilly and Co,
Indianapolis, IN, 46285, USA
SOURCE: Drug Metabolism Reviews, (August 2004) Vol. 36, No. Suppl.
1, pp. 342. print.
Meeting Info.: 7th International Meeting of the
International Society for the Study of Xenobiotics.
Vancouver, BC, Canada. August 29-September 02, 2004.
International Society for the Study of Xenobiotics.
ISSN: 0360-2532 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 May 2005
Last Updated on STN: 25 May 2005
CONCEPT CODE: General biology - Symposia, transactions and proceedings
00520
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and
pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids
10064
Enzymes - General and comparative studies: coenzymes
10802
Pathology - Therapy 12512
Digestive system - Physiology and biochemistry 14004
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008
Pharmacology - Cardiovascular system 22010
Immunology - General and methods 34502
INDEX TERMS: Major Concepts
Digestive System (Ingestion and Assimilation);
Enzymology (Biochemistry and Molecular Biophysics);
Pharmacology
INDEX TERMS: Parts, Structures, & Systems of Organisms
liver microsome: digestive system
INDEX TERMS: Chemicals & Biochemicals
CS-747 [LY640315]: antithrombotic-drug,
cardiovascular-drug, hematologic-drug, novel
thienopyridine anti-platelet agent, biotransformation;
CYP2C19; CYP2C9; CYP3A; GSH; NADPH; R-138727; R-95913;
cDNA [complementary DNA]; cytochrome P450 [EC
1.14.14.1]; dithiothreitol; monoclonal antibodies;
reduced glutathione; sodium phosphate buffer
INDEX TERMS: Methods & Equipment

Michaelis-Menten kinetics: mathematical and computer techniques

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

REGISTRY NUMBER: 150322-43-3 (CS-747)
150322-43-3 (LY640315)
70-18-8 (GSH)
53-57-6 (NADPH)
9035-51-2 (cytochrome P450)
9038-14-6 (cytochrome P450)
9035-51-2 (EC 1.14.14.1)
9038-14-6 (EC 1.14.14.1)
3483-12-3 (dithiothreitol)
70-18-8 (reduced glutathione)

L53 ANSWER 17 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:190908 BIOSIS
DOCUMENT NUMBER: PREV200500192774
TITLE: The disposition of CS-747 (LY640315), a novel thienopyridine, in mice.
AUTHOR(S): Gillespie, Todd A. [Reprint Author]; Smith, Richard L.; Rash, T. James; Ikeda, Toshihiko; Farid, Nagy A.
CORPORATE SOURCE: Div Drug Disposit, Lilly Res Labs, Indianapolis, IN, 46285, USA
SOURCE: Drug Metabolism Reviews, (August 2004) Vol. 36, No. Suppl. 1, pp. 242. print.
Meeting Info.: 7th International Meeting of the International Society for the Study of Xenobiotics. Vancouver, BC, Canada. August 29-September 02, 2004. International Society for the Study of Xenobiotics. ISSN: 0360-2532 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 May 2005
Last Updated on STN: 25 May 2005
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Pathology - Therapy 12512
Metabolism - General metabolism and metabolic pathways 13002
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Drug metabolism and metabolic stimulators 22003

INDEX TERMS: Major Concepts
Metabolism; Pharmaceuticals (Pharmacology)
INDEX TERMS: Parts, Structures, & Systems of Organisms
plasma: blood and lymphatics
INDEX TERMS: Chemicals & Biochemicals
CS-747 [LY640315]: metabolic-drug, oral administration,

pharmacokinetics, thienopyridine, disposition,
pharmaceutical

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates,
Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 150322-43-3 (CS-747)
150322-43-3 (LY640315)

L53 ANSWER 18 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN

ACCESSION NUMBER: 2004:2929 BIOSIS
DOCUMENT NUMBER: PREV200400005090
TITLE: ADP receptors-targets for developing antithrombotic agents.
AUTHOR(S): Kunapuli, Satya P. [Reprint Author]; Ding, Zhongren;
Dorsam, Robert T.; Kim, Soochong; Murugappan, Swaminathan;
Quinton, Todd M.
CORPORATE SOURCE: Department of Physiology, Temple University Medical School,
3420 North Broad Street, Rm. 224OMS, Philadelphia, PA,
19140, USA
spk@temple.edu
SOURCE: Current Pharmaceutical Design, (2003) Vol. 9, No. 28, pp.
2303-2316. print.
ISSN: 1381-6128 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Dec 2003
Last Updated on STN: 17 Dec 2003
CONCEPT CODE: Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and
pyrimidines 10062
Biophysics - Membrane phenomena 10508
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Blood and hematopoietic agents 22008
INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation);
Cardiovascular System (Transport and Circulation);
Pharmacology
INDEX TERMS: Parts, Structures, & Systems of Organisms
platelet: blood and lymphatics
INDEX TERMS: Chemicals & Biochemicals
ADP; CS-747: P2Y12 antagonist; P2X1; P2Y1; P2Y12;
calcium channel; clopidogrel: hematologic-drug; platelet
P2 receptor; ticlopidine: anticoagulant-drug,
hematologic-drug
INDEX TERMS: Methods & Equipment
antithrombotic treatment: clinical techniques, therapeutic
and prophylactic techniques
INDEX TERMS: Miscellaneous Descriptors
platelet aggregation

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common): animal model
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates,
Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 58-64-0Q (ADP)
4792-83-0Q (ADP)
7722-76-1Q (ADP)
19429-39-1Q (ADP)
175832-20-9Q (ADP)
150322-43-3 (CS-747)
113665-84-2 (clopidogrel)
55142-85-3 (ticlopidine)

L53 ANSWER 19 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN

ACCESSION NUMBER: 2002:313326 BIOSIS
DOCUMENT NUMBER: PREV200200313326
TITLE: Platelet inhibitory effects of R-138727 the active
metabolite of CS-747 a potent thienopyridyl P2Y12
antagonist prodrug.

AUTHOR(S): Jakubowski, Joseph A. [Reprint author]; Ogawa, Taketoshi;
Sugidachi, Atsuhiko; Yoneda, Kenji; Iwamura, Ryo; Inoue,
Teruhiko; Kimura, Tomio; Asai, Fumitoshi

CORPORATE SOURCE: BioMolecular Pharmacology, Eli Lilly and Company, Lilly
Corporate Center, Indianapolis, IN, 46285, USA

SOURCE: FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A203.
print.
Meeting Info.: Annual Meeting of the Professional Research
Scientists on Experimental Biology. New Orleans, Louisiana,
USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 29 May 2002
Last Updated on STN: 29 May 2002

ABSTRACT: CS-747 is a thienopyridyl prodrug that is metabolized in vivo to an
active platelet-inhibitory metabolite. We have identified R-138727 as an
active metabolite of CS-747 and a potent antagonist of the P2Y12 platelet ADP
receptor. In vitro studies were performed to evaluate the platelet inhibitory
effects of R-138727. In human platelets, R-138727 inhibited ADP- and
2-MeS-ADP-induced platelet aggregation in a concentration- and time-dependent
manner. R-138727 also inhibited collagen- and arachidonic acid-induced
platelet aggregation but demonstrated minimal inhibition of thrombin
peptide-induced aggregation. R-138727 consists of four optical isomers, and
the previously described platelet-inhibitory metabolite R-99224 is a component
of R-138727. While all the isomers of R-138727 inhibited ADP-induced platelet
aggregation, the R,S enantiomer R-125690 was the most potent. The
antiaggregatory potency of R-138727 was very similar to that of R-99224. These
results show that R-138727 is an active metabolite of CS-747 and is a potent
inhibitor of platelet aggregation. These observations are consistent with the
effective antithrombotic activities that CS-747 provides following oral dosing.

CONCEPT CODE: General biology - Symposia, transactions and proceedings
00520
Pathology - Therapy 12512

Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Blood and hematopoietic agents 22008
Tissue culture, apparatus, methods and media 32500

INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation);
Pharmacology

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelets: blood and lymphatics, drug treatment,
in-vitro culture

INDEX TERMS: Chemicals & Biochemicals
R 138727: hematologic-drug, CS 747 metabolite, platelet
aggregation inhibitor; thienopyridyl prodrug [CS 747]:
hematologic-drug, platelet P-2Y-12 ADP receptor
antagonist, platelet aggregation inhibitor

INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: normal blood donors
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates,
Vertebrates

REGISTRY NUMBER: 150322-43-3 (CS 747)

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ACCESSION NUMBER: 2001:576047 BIOSIS
DOCUMENT NUMBER: PREV200100576047
TITLE: CS-747 and R-99224. Platelet antiaggregatory, P2T
antagonist.

AUTHOR(S): Doggrell, S. A. [Reprint author]; Mealy, N. E.; Castaner,
J.

CORPORATE SOURCE: Department of Physiology and Pharmacology, The University
of Queensland, Brisbane, Qld, 4072, Australia

SOURCE: Drugs of the Future, (September, 2001) Vol. 26, No. 9, pp.
835-840. print.
ISSN: 0377-8282.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 2001
Last Updated on STN: 25 Feb 2002

CONCEPT CODE: Biochemistry studies - Nucleic acids, purines and
pyrimidines 10062
Pathology - Therapy 12512
Cardiovascular system - Blood vessel pathology 14508
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Cardiovascular system 22010

INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation);
Pharmacology

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelets: blood and lymphatics, shape change

INDEX TERMS: Diseases
vascular injury: injury, vascular disease

INDEX TERMS: Chemicals & Biochemicals
ADP: platelet agonist; CS-747: cardiovascular-drug, P2T antagonist, platelet antiaggregatory, synthesis;
R-99224: cardiovascular-drug, P2T antagonist, platelet antiaggregatory, synthesis; granule contents: secretion

INDEX TERMS: Miscellaneous Descriptors
bloodstream

REGISTRY NUMBER: 58-64-0Q (ADP)
4792-83-0Q (ADP)
7722-76-1Q (ADP)
19429-39-1Q (ADP)
175832-20-9Q (ADP)
150322-43-3 (CS-747)
204204-74-0 (R-99224)

L53 ANSWER 21 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
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ACCESSION NUMBER: 2001:160957 BIOSIS
DOCUMENT NUMBER: PREV200100160957
TITLE: Antiplatelet action of R-99224, an active metabolite of a novel thienopyridine-type Gi-linked P2T antagonist, CS-747.
AUTHOR(S): Sugidachi, Atsuhiko; Asai, Fumitoshi [Reprint author]; Yoneda, Kenji; Iwamura, Ryo; Ogawa, Taketoshi; Otsuguro, Ken-ichi; Koike, Hiroyuki
CORPORATE SOURCE: Pharmacology and Molecular Biology Research Laboratories, Sankyo Co., Ltd., 1-2-58 Hiromachi, Shinagawa-ku, Tokyo, 140-8710, Japan
toasai@shina.sankyo.cp.jp
SOURCE: British Journal of Pharmacology, (January, 2001) Vol. 132, No. 1, pp. 47-54. print.
CODEN: BJPCBM. ISSN: 0007-1188.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Mar 2001
Last Updated on STN: 15 Feb 2002

ABSTRACT:1 CS-747 is a novel thienopyridine-type platelet ADP inhibitor which lacks in vitro activity. This study examined pharmacological profiles of R-99224, a hepatic metabolite of CS-747. 2 R-99224 produced a concentration-dependent inhibition of in vitro platelet aggregation in washed human platelets (0.03-1 $\mu\text{g ml}^{-1}$), which was relatively specific to ADP compared to collagen and thrombin. 3 R-99224 (0.1 - 3 $\mu\text{g ml}^{-1}$) also elicited a similar inhibition of ADP-induced aggregation in rat platelets. The inhibition by R-99224 (10 $\mu\text{g ml}^{-1}$) persisted even after platelets were washed three times. Intravenous injection of R-99224 (0.1 - 3 mg kg^{-1}) to rats resulted in a dose-dependent inhibition of ex vivo ADP-induced platelet aggregation. 4 R-99224 (0.1 - 100 μM) decreased binding of (3H)-2-methylthio-ADP((3H)-2-MeS-ADP), a stable ligand for platelet ADP receptors, to washed human platelets. The inhibition by R-99224 reached a plateau at a concentration of 3 μM (1.4 $\mu\text{g ml}^{-1}$), but complete inhibition was not achieved even at the highest concentration used (100 μM). 5 R-99224 (10 μM) in combination with ARL-66096 (0.3 μM), an ATP analogue-type Gi-linked P2T receptor antagonist, produced no additional inhibition of (3H)-2-MeS-ADP binding. In contrast, (3H)-2-MeS-ADP binding was completely abolished by R-99224 (10 μM) in combination with A3P5PS (300 μM), a selective P2Y1 antagonist, suggesting that R-99224 selectively binds to the Gi-linked P2T receptor. 6 R-99224 (0.01 - 3 $\mu\text{g ml}^{-1}$) inhibited ADP-induced (125I)-fibrinogen binding to human platelets in a concentration-dependent manner. R-99224 (0.1 - 1 $\mu\text{g ml}^{-1}$) also inhibited the ADP-induced decrease in cyclic AMP levels in PGE1-stimulated platelets, whereas

the agent did not affect ADP (10 μ M)-induced Ca^{2+} mobilization. 7 These findings suggest that R-99224 is a selective and irreversible antagonist of G_i -linked P2T receptors and that R-99224 is a responsible molecule for in vivo actions of CS-747.

CONCEPT CODE: Pharmacology - Blood and hematopoietic agents 22008
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005

INDEX TERMS: Major Concepts
Pharmacology; Blood and Lymphatics (Transport and Circulation)

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelet: blood and lymphatics, aggregation, inhibition

INDEX TERMS: Chemicals & Biochemicals
CS-747: anticoagulant-drug, thienopyridine-type
G-i-linked P2T antagonist; G-i-linked P2T receptors;
R-99224: Cs-747 metabolite, antiplatelet action

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Sprague-Dawley rat: male
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 150322-43-3 (CS-747)
204204-74-0 (R-99224)

L53 ANSWER 22 OF 56 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:235332 BIOSIS

DOCUMENT NUMBER: PREV200000235332

TITLE: The in vivo pharmacological profile of CS-747, a novel antiplatelet agent with platelet ADP receptor antagonist properties.

AUTHOR(S): Sugidachi, Atsuhiko; Asai, Fumitoshi [Reprint author]; Ogawa, Taketoshi; Inoue, Teruhiko; Koike, Hiroyuki

CORPORATE SOURCE: Pharmacology and Molecular Biology Research Laboratories, Sankyo Co., Ltd, 1-2-58 Hiromachi, Shinagawa-ku, Tokyo, 140-8710, Japan

SOURCE: British Journal of Pharmacology, (April, 2000) Vol. 129, No. 7, pp. 1439-1446. print.

CODEN: BJPCBM. ISSN: 0007-1188.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 7 Jun 2000

Last Updated on STN: 5 Jan 2002

ABSTRACT:1 CS-747 is a novel antiplatelet agent that generates an active

metabolite, R-99224, in vivo. CS-747 itself was totally inactive in vitro. This study examined in vitro pharmacological profiles of CS-747 after single oral administration to rats. 2 Orally administered CS-747 (0.3-10 mg kg⁻¹) partially but significantly decreased (3H)-2-methylthio-ADP binding to rat platelets. CS-747 (3 mg kg⁻¹, p.o.) treatment neutralized ADP-induced decreases of cyclic AMP concentrations induced by prostaglandin E₁, suggesting that metabolites of CS-747 interfere with Gi-linked P₂T receptor. 3 CS-747 (0.3 and 3 mg kg⁻¹, p.o.) markedly inhibited ex vivo washed platelet aggregation in response to ADP but not to thrombin. CS-747 also exhibited a marked inhibition of ADP-induced ex vivo platelet aggregation in PRP with a rapid onset (<0.5 h) and long duration (>3 days) of action (ED₅₀ at 4 h=1.2 mg kg⁻¹). 4 R-99224 (IC₅₀=45 µM) inhibited in vitro PRP aggregation in a concentration-related manner. 5 CS-747 prevented thrombus formation in a dose-related manner with an ED₅₀ value of 0.68 mg kg⁻¹. CS-747 was more potent than clopidogrel (6.2 mg kg⁻¹) and ticlopidine (>300 mg kg⁻¹). 6 CS-747, clopidogrel, and ticlopidine prolonged the bleeding time. The order of potency of these agents in this activity was the same as that in antiaggregatory and antithrombotic activities. 7 These findings indicate that CS-747 is an orally active and a potent antiplatelet and antithrombotic agent with a rapid onset and long duration of action, and warrants clinical evaluations of the agent.

CONCEPT CODE: Pharmacology - General 22002
Cytology - Animal 02506
Biochemistry studies - General 10060
Metabolism - General metabolism and metabolic pathways 13002
Cardiovascular system - General and methods 14501
Blood - General and methods 15001

INDEX TERMS: Major Concepts
Pharmacology; Blood and Lymphatics (Transport and Circulation)

INDEX TERMS: Parts, Structures, & Systems of Organisms
platelet: blood and lymphatics

INDEX TERMS: Chemicals & Biochemicals
ADP; CS-747: anticoagulant-drug, hematologic-drug, antiplatelet agent, pharmacological profile; R-99224: metabolite; clopidogrel; cyclic AMP; prostaglandin E-1; thrombin; ticlopidine

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Sprague-Dawley rat: male
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 58-64-0Q (ADP)
4792-83-0Q (ADP)
7722-76-1Q (ADP)
19429-39-1Q (ADP)
175832-20-9Q (ADP)
150322-43-3 (CS-747)
204204-74-0 (R-99224)
113665-84-2 (clopidogrel)
60-92-4 (cyclic AMP)
745-65-3 (prostaglandin E-1)
9002-04-4 (thrombin)
55142-85-3 (ticlopidine)

STN

ACCESSION NUMBER: 1999:191247 BIOSIS
DOCUMENT NUMBER: PREV199900191247
TITLE: Efficacy of CS-747, a new potent antiplatelet agent.
AUTHOR(S): Hirota, T. [Reprint author]; Sugii, H.; Asai, F.; Kawabata, K.; Inoue, T.; Iwamura, R.; Freestone, S.; Dickson, J.
CORPORATE SOURCE: Sankyo Co. Ltd., Ube Industries Ltd., Tokyo, Japan
SOURCE: Clinical Pharmacology and Therapeutics, (Feb., 1999) Vol. 65, No. 2, pp. 148. print.
Meeting Info.: One-hundredth Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics. San Antonio, Texas, USA. March 18-20, 1999. American Society for Clinical Pharmacology and Therapeutics.
CODEN: CLPTAT. ISSN: 0009-9236.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999
CONCEPT CODE: Pharmacology - General 22002
Metabolism - General metabolism and metabolic pathways 13002
Cardiovascular system - General and methods 14501
General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - General 10060
INDEX TERMS: Major Concepts
Cardiovascular System (Transport and Circulation);
Pharmacology
INDEX TERMS: Diseases
angina: heart disease
Angina Pectoris (MeSH)
INDEX TERMS: Diseases
myocardial infarction: heart disease, vascular disease
Myocardial Infarction (MeSH)
INDEX TERMS: Diseases
stroke: nervous system disease, vascular disease
Cerebrovascular Disorders (MeSH)
INDEX TERMS: Chemicals & Biochemicals
CS-747: antiplatelet agent, efficacy
INDEX TERMS: Miscellaneous Descriptors
pharmacokinetics; Meeting Abstract
REGISTRY NUMBER: 150322-43-3 (CS-747)

L53 ANSWER 24 OF 56 TOXCENTER COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:124751 TOXCENTER
COPYRIGHT: Copyright 2006 ACS
DOCUMENT NUMBER: CA14413226296E
TITLE: Oral prophylactic agents for thrombosis and embolism
AUTHOR(S): Morishima, Yoshiyuki; Watanabe, Kengo
CORPORATE SOURCE: ASSIGNEE: Daiichi Seiyaku Co., Ltd.
PATENT INFORMATION: JP 200652208 A2 23 Feb 2006
SOURCE: (2006) Jpn. Kokai Tokkyo Koho, 29 pp.
CODEN: JKXXAF.
COUNTRY: JAPAN
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2006:170095
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 14 Mar 2006

Last Updated on STN: 9 May 2006

ABSTRACT:

Title agents contain diamines I [Q1 = (un)substituted 4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl, 4,5,6,7-tetrahydrothiazolo[4,5-c]pyridin-2-yl, 4,5,6,7-tetrahydrothieno[2,3-c]pyridin-2-yl, 4,5,6,7-tetrahydrooxazolo[5,4-c]pyridin-2-yl, 4,6-dihydro-5H-pyrrolo[3,4-d]thiazol-2-yl, etc.; Q2 = C1-8 alkylene, (CH₂)_p(CH₂)_q (p, q = 1-3; p + q = 2-4); A = O, N, S, SO, SO₂, NH; R1, R2 = H, OH, NH₂, CO₂H, (halo)alkyl, acyl, alkoxy carbonylalkyl, (un)substituted acylamino, (un)substituted 3- to 6-membered heterocyclylcarbonyl, etc.; Q3 = CO, SO₂, COCONH, CSCONH, COCSNH, CSCSNH; Q4 = (un)substituted Ph, naphthyl, pyridyl, pyrimidyl, indolyl, benzothienyl, furyl, etc.] and antiplatelet agents chosen from aspirin, sarpogrelate, limaprost, cilostazol, and piperidines II or III [R101, R105 = H, lower alkyl, lower alkoxy carbonyl, lower alkylcarbonyl; R102, R103, R106, R107 = H, lower alkyl, halo; R104 = H, OH, lower alkylcarbonyloxy; R108 = H, lower alkyl; R109 = H, lower alkylcarbonyl] as active ingredients. Thus, combination use of N1-(5-chloropyridin-2-yl)-N2-[(1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-[[[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino]cyclohexyl]ethanediamide HCl salt (IV) and ticlopidine prevented 75% thrombosis formation in rats. CYP2D6- and CYP3A4-dependent metabolism of IV was 0.1-0.81 pmol/pmol/CYP/min, suggesting nonsusceptibility of IV to the enzymes.

CLASSIFICATION CODE: 1-8

SUPPLEMENTARY TERMS: Miscellaneous Descriptors

oral prophylaxis antithrombotic antiplatelet combination;
ticlopidine cyclohexylethanediamide combination
antithrombotic oral prophylaxis

REGISTRY NUMBER:

50-78-2 (Aspirin)
50-78-2Q (Aspirin, mixts. contg.)
55142-85-3 (Ticlopidine)
55142-85-3Q (Ticlopidine, mixts. contg.)
73963-72-1 (Cilostazol)
73963-72-1Q (Cilostazol, mixts. contg.)
74397-12-9 (Limaprost)
74397-12-9Q (Limaprost, mixts. contg.)
113665-84-2 (Clopidogrel)
113665-84-2Q (Clopidogrel, mixts. contg.)
125926-17-2 (Sarpogrelate)
125926-17-2Q (Sarpogrelate, mixts. contg.)
150322-43-3Q (mixts. contg.)

REGISTRY NUMBER:

480448-29-1; 150322-43-3

L53 ANSWER 25 OF 56 TOXCENTER COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:260164 TOXCENTER

COPYRIGHT: Copyright (c) 2006 The Thomson Corporation

DOCUMENT NUMBER: 42-17755

TITLE: Randomized comparison of Prasugrel (CS- 747, LY640315), a novel thienopyridine P2Y₁₂ antagonist, with clopidogrel in percutaneous coronary intervention - Results of the joint utilization of medications to block platelets optimally (JUMBO)-TIMI 26 trial

AUTHOR(S): Wiviott, SD; Antman, EM; Winters, KJ; Weerakkody, G; JUMBO-TIMI 26 Investigators; et al

CORPORATE SOURCE: Harvard Univ, Div Cardiovasc, 75 Francis St, Boston, MA 02115, USA swiviott@partners.org

SOURCE: Circulation, (2005) Vol. 111, pp. 3366-3373. 31 Refs. CODEN: CIRCAZ. ISSN: 0009-7322.

DOCUMENT TYPE: Journal

FILE SEGMENT: IPA

OTHER SOURCE: IPA 2005:17729

LANGUAGE: English
ENTRY DATE: Entered STN: 4 Oct 2005
Last Updated on STN: 4 Oct 2005

ABSTRACT:

To compare the antiplatelet efficacy and safety of prasugrel (CS-747, LY-640315) with clopidogrel in percutaneous coronary intervention, a phase II clinical study was performed. Patients (n=904) were randomized to either standard dosing with or 1 of 3 prasugrel regimens. Subjects were monitored for 30 days for bleeding and clinical events. Hemorrhagic complications were infrequent, with no significant difference between patients treated with prasugrel or clopidogrel in the rate of significant bleeding.

SECTION CODE: 5 Investigational Drugs; 4 Toxicity
CLASSIFICATION CODE: 20:12.04 Platelet aggregation inhibitors; 20:12.04
Platelet aggregation inhibitors

SUPPLEMENTARY TERMS: Miscellaneous Descriptors
CS-747; coronary disease
Clopidogrel; coronary disease
Platelet aggregation inhibitors; cs-747
Platelet aggregation inhibitors; clopidogrel
Drug comparisons; cs-747 and clopidogrel
Drug comparisons; clopidogrel and cs-747
Dosage; cs-747
Toxicity; cs-747
Coronary disease; cs-747
Dosage; clopidogrel
Toxicity; clopidogrel
Coronary disease; clopidogrel
Drugs; new
Interventions; coronary disease

REGISTRY NUMBER: 150322-43-3 (CS-747)
113665-84-2 (Clopidogrel)
CHEMICAL NAME: CS-747 (Prasugrel); CS-747 (LY-640315)

L53 ANSWER 26 OF 56 TOXCENTER COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:10603 TOXCENTER
COPYRIGHT: Copyright 2006 ACS
DOCUMENT NUMBER: CA13607096057Z
TITLE: Tetrahydrothienopyridine derivative acid addition salts
AUTHOR(S): Asai, Fumitoshi; Ogawa, Taketoshi; Naganuma, Hideo;
Yamamura, Naotoshi; Inoue, Teruhiko; Nakamura, Kazuyoshi
CORPORATE SOURCE: ASSIGNEE: Ube Industries, Ltd.
PATENT INFORMATION: WO 2002004461 A1 17 Jan 2002
SOURCE: (2002) PCT Int. Appl., 33 pp.
CODEN: PIXXD2.
COUNTRY: JAPAN
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2002:51473
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 22 Jan 2002
Last Updated on STN: 9 Dec 2003

ABSTRACT:

Claimed are acid addition salts of 2-acetoxy-5-(α -cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine. These acid addition salts exhibit excellent peroral absorbability, metabolism-activating and platelet aggregation-inhibiting effects, low toxicity, and excellent storage and handling stabilities, and are useful as drugs for thrombosis and infarction. Oral administration of 2-acetoxy-5-(α -cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine maleic acid salt at 0.3 mg/kg to dogs gave $58.6 \pm 15.7\%$ inhibition of platelet aggregation at 4 h after said

administration, vs. 23.8±12.6% platelet aggregation inhibition caused by 2-acetoxy-5-(α -cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine (free base) at 0.3 mg/kg orally. Formulations are given.

CLASSIFICATION CODE: 1-8

SUPPLEMENTARY TERMS: Miscellaneous Descriptors
tetrahydrothienopyridine deriv acid salt thrombosis
infarction remedy

REGISTRY NUMBER: 108-24-7 (Acetic anhydride)
110-16-7 (Maleic acid)
446-48-0 (2-Fluorobenzyl bromide)
5500-21-0 (Cyclopropyl cyanide)
7439-95-4 (Magnesium)
7647-01-0 (Hydrochloric acid)
67-64-1 (Acetone)

REGISTRY NUMBER: 389574-19-0; 389574-20-3;
150322-43-3; 115473-15-9; 150322-38-6;
150322-73-9; 204205-33-4

L53 ANSWER 27 OF 56 TOXCENTER COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:143127 TOXCENTER

COPYRIGHT: Copyright 2006 ACS

DOCUMENT NUMBER: CA13314187474N

TITLE: CS-747, a new platelet ADP receptor antagonist

AUTHOR(S): Asai, Fumitoshi; Konse, Tomonori; Sugidachi, Atsuhiko;

Ikeda, Toshihiko; Sanbuissho, Atsushi; Hirota, Takashi

CORPORATE SOURCE: Pharmacology and Molecular Biology Research Laboratories,
Product Development Laboratories, SANKYO CO., LTD., Tokyo,
140-8710, Japan.

SOURCE: Annual Report of Sankyo Research Laboratories, (1999) Vol.
51, pp. 1-44.

CODEN: ASRLEC. ISSN: 1341-741X.

COUNTRY: JAPAN

DOCUMENT TYPE: Journal

FILE SEGMENT: CAPLUS

OTHER SOURCE: CAPLUS 2000:288118

LANGUAGE: English

ENTRY DATE: Entered STN: 16 Nov 2001

Last Updated on STN: 26 Mar 2002

ABSTRACT:

A review with 29 refs. on physicochem. properties and pharmacol. of the title antiplatelet agent.

CLASSIFICATION CODE: 1-0

SUPPLEMENTARY TERMS: Miscellaneous Descriptors
review platelet ADP receptor antagonist CS747 antiplatelet

REGISTRY NUMBER: 150322-43-3 (CS 747)

L53 ANSWER 28 OF 56 TOXCENTER COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:104474 TOXCENTER

COPYRIGHT: Copyright 2006 ACS

DOCUMENT NUMBER: CA12808093213W

TITLE: Novel medicinal compositions of hydropyridines

AUTHOR(S): Asai, Fumitoshi; Ogawa, Taketoshi; Inoue, Teruhiko

CORPORATE SOURCE: ASSIGNEE: Ube Industries, Ltd.

PATENT INFORMATION: WO 9749397 A1 31 Dec 1997

SOURCE: (1997) PCT Int. Appl., 47 pp.

CODEN: PIXXD2.

COUNTRY: JAPAN

DOCUMENT TYPE: Patent

FILE SEGMENT: CAPLUS

OTHER SOURCE: CAPLUS 1998:42276
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 9 Mar 2004

ABSTRACT:

The invention relates to compns. containing as the active ingredient 4,5,6,7-tetrahydrothieno[3,2-c]pyridines represented by the following general formula : R1-CH(R2)-R3 or pharmacol. acceptable salts thereof which have an excellent effect of inhibiting the progression of arteriosclerosis and a low toxicity and, therefore, are highly useful as remedies or preventives for arteriosclerosis. In said formula, R1 represents optionally substituted phenyl; R2 represents H, alkoxycarbonyl or optionally substituted aliphatic acyl; and R3 represents optionally substituted 4,5,6,7-tetrahydrothieno[3,2-c]pyridin-5-yl.

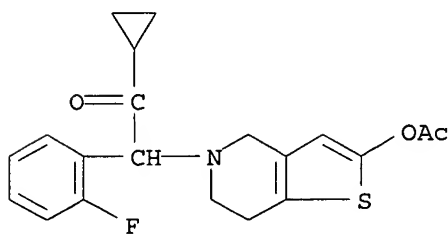
CLASSIFICATION CODE: 63-6

SUPPLEMENTARY TERMS: Miscellaneous Descriptors

antiarteriosclerotic hydropyridine pharmaceutical
REGISTRY NUMBER: 90055-48-4; 90055-76-8; 109904-27-0; 109904-29-2;
150322-13-7; 150322-15-9; 150322-19-3; 150322-38-6;
150322-40-0; 150322-42-2; **150322-43-3**;
150322-44-4; 150322-45-5; 150322-46-6; 150322-51-3;
150322-59-1; 150322-62-6; 150322-63-7; 150322-64-8;
150322-65-9; 178688-44-3; 201049-72-1; 201049-73-2;
201049-74-3; 201049-75-4; 201049-76-5; 201049-77-6;
201049-78-7

L53 ANSWER 29 OF 56 IMSRESEARCH COPYRIGHT 2006 IMSWORLD on STN

ACCESSION NUMBER: 1998:226 IMSRESEARCH
SOURCE: R&D Focus, (8 May 2006)
GENERIC NAME: prasugrel
REFERENCE: pINN
LABORATORY NAME: CS 747; LY 640315
CHEMICAL NAME: 2-[2-(acetyloxy)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-cyclop ropyl-2-(2-fluorophenyl)ethanone
CAS REGISTRY NO.: **150322-43-3**
STRUCTURE:



DERIVATIVE(S): **150322-43-3**prasugrel
CLASSIFICATION: B1C Platelet Aggregation Inhibitors; C1D Coronary Therapy
INDICATION: coronary artery disease; thrombosis; cardiovascular disease; stroke; ischemia; myocardial infarction; heart ischemia; angina
ACTION: platelet antiaggregant; purinoceptor antagonist
HIGHEST DEV. PHASE: Phase III (50)
LATEST INFORMATION: UPDATE: Analyst prediction.In a presentation at Lilly's Investment Community Update, 9 December 2004, New

York, USA, Steven Paul, Executive VP, Science & Technology at Lilly, announced that Lilly and Sankyo have initiated enrollment of a multicenter, worldwide, phase III trial, known as TRITON-TIMI 38, of prasugrel. The trial is expected to enroll over 13 000 patients with acute coronary syndrome (heart attacks and/or unstable angina) who are to undergo percutaneous coronary intervention (PCI). Lilly anticipates an NDA submission in the USA late 2006 for the treatment of acute coronary syndrome. Prasugrel, an oral antithrombotic prodrug, inhibits the ADP receptor.

CURRENT DEVELOPMENT STATUS:

Type	Status	Stage	Region	Indication
Highest Phase	Phase III	50		
Phase	Phase III		Worldwide	coronary artery disease
Phase	Phase II		United States	ischemia
Phase	Phase II		Europe	ischemia
Phase	Phase I		Japan	ischemia

COMPANY INFORMATION:

Type	Company	Nationality
Originator	Daiichi Sankyo	Japan
Co-developer	Ube	Japan
Other	Lilly	United States
Assignee	Sankyo : Ube	

ESTIMATED LAUNCH:	2007	United States
	2007	Europe

PATENT SUMMARY:

Product: EP 542411 B 1998, priority JP 227875 1991, designating 17 states. Equivalents identified in 17 countries.

COMMERCIAL SUMMARY:

Prasugrel, an oral antithrombotic prodrug discovered by Daiichi Sankyo (formerly known as Sankyo) and Ube, inhibits the ADP receptor and is being developed for use in the treatment of acute coronary syndrome in patients who have suffered a heart attack or have angina. Lilly and Daiichi Sankyo have initiated an international phase III trial of prasugrel in conjunction with Harvard Medical School (USA) and Brigham and Women's Hospital (USA) (Lilly, DEC 2004). The trial, designated TRITON-TIMI 38, aims to enroll 13 000 patients with acute coronary syndrome (heart attacks and/or unstable angina), who are to undergo percutaneous coronary intervention (PCI). The aim of the trial is to evaluate the ability of prasugrel to prevent heart attack, stroke and death in patients who undergo PCI compared with clopidogrel. The secondary endpoints include impact on bleeding, recurrent ischemia and need for additional procedures to restore blood flow (Lilly, Sankyo, OCT 2004). Lilly has completed a multicenter, interventional phase II trial in the USA, which compared

prasugrel with clopidogrel in 904 patients aged 18-75 years undergoing percutaneous coronary intervention (PCI) (Lilly, FEB 2004) and results have been reported (Lilly, Sankyo, AUG 2004). Lilly anticipates filing a regulatory submission for marketing approval in the second half of 2007 (Lilly, DEC 2005). Lilly was planning to conduct phase III trials of the agent in acute coronary syndrome and stroke, and dependent on a successful outcome, expected a regulatory submission in the USA late 2006 (Lilly, DEC 2004). Phase II trials are under way in Europe and the USA under co-development with Lilly to evaluate the agent as a treatment for ischemic disease (Sankyo, JAN 2004). Phase II trials were planned to commence second quarter 2003 for acute coronary syndrome and cerebrovascular accident (Sankyo, FEB 2003). Phase I trials have been conducted in Japan, the USA (Sankyo, JUN 2002) and Europe (Sankyo, NOV 1999). The product is also to be developed for secondary prevention of thrombotic cardiovascular complications in patients with recent ischemic stroke or unstable angina and myocardial infarction, as well as for reducing secondary complications such as myocardial infarction, recurrent stroke and rehospitalization for severe angina. Sankyo (now known as Daiichi Sankyo) and Lilly have signed a letter of intent, under which Sankyo will receive a signing fee, milestone payments and royalties on product sales. Under the proposed agreement, prasugrel will be co-marketed by Lilly and Sankyo except in certain countries where Lilly will receive exclusive sales and marketing rights. The product will be co-promoted by both companies in the USA. Additionally, both companies plan to share in the development of the compound, whilst Ube will manufacture the bulk material (Lilly, DEC 2000). Daiichi Sankyo predicts launches for the product in the USA and Europe during 2007 with peak sales of around YEN100 billion (Sankyo, MAY 2002). (Ube review ed, AUG 1998; Sankyo confirmed phase I, Japan, ischemic disease, JAN 2004; Sankyo confirmed phase III ongoing, worldwide, acute coronary syndrome, MAY 2005) Latest prediction Analyst, Credit Suisse, reporting on Lilly, predicts the release of data from a phase III trial of prasugrel first half 2007; estimates sales of US\$240.1 million in 2008, US\$567.1 million in 2009 and US\$992.7 million in 2010 (Credit Suisse, APR 2006). >Bear Stearns Analyst, Bear Stearns, reporting on Lilly, estimates worldwide sales for prasugrel of US\$300 million in 2008, US\$609 million in 2009 and US\$1.041 billion in 2010 (Bear Stearns, SEP 2005). Credit Suisse First Boston Analyst, Credit Suisse First Boston, reporting on Daiichi Sankyo, estimates sales for CS 747 (prasugrel) of YEN950 billion in FYE March 2009 (Credit Suisse First Boston, DEC 2005). >Analyst, Credit Suisse First Boston, reporting on Lilly, estimates sales for prasugrel of US\$214.6 million in 2007 and US\$1.226 billion in 2010 (Credit Suisse First Boston, JUN 2005). >Analyst, Credit Suisse First Boston, reporting on Lilly, predicts a 2007 launch for prasugrel and estimates peak sales of US\$1.5 billion (Credit Suisse First Boston, DEC 2004). JPMorgan Analyst, JPMorgan, reporting on Sankyo (now known as Daiichi Sankyo), predicts a regulatory filing for CS 747 (prasugrel) first half 2007 and estimates sales of YEN15 billion in FYE March 2009 and peak sales of over YEN100 billion (JPMorgan, NOV 2004). Merrill Lynch Analyst, Merrill Lynch, predicts a launch in 2006 (Merrill Lynch, JUN 2002). Morgan Stanley Analyst, Morgan Stanley, reporting on Daiichi Sankyo, estimates total sales for CS 747 (prasugrel) of YEN10.7 billion in FY2008 and YEN21 billion in FY2009 (Morgan Stanley, SEP 2005). >Analyst, Morgan Stanley, reporting on Sankyo (now known as Daiichi Sankyo) predicts a regulatory filing for CS 747 (prasugrel) in 2006 (Morgan Stanley, MAR 2005). Analyst, Morgan Stanley, reporting on Lilly, estimates sales for prasugrel of US\$100 million in 2008 (Morgan Stanley, APR 2004). >Analyst, Morgan Stanley, reporting on Lilly, estimates sales for prasugrel of US\$100 million in 2008 and US\$350 million in 2009 (Morgan Stanley, OCT 2005).

SCIENTIFIC SUMMARY:

Preclinical studies showed that prasugrel was metabolized to its active component efficiently (Lilly, FEB 2004). In clinical studies, prasugrel demonstrated a high level of platelet inhibition (Lilly, FEB 2004). Results

from a phase II trial comparing prasugrel to clopidogrel, involving 904 patients who had suffered a heart attack or heart-related chest pain, showed a non-significant reduction in major adverse cardiovascular events (death, heart attack and stroke), in patients treated with prasugrel for 30 days, compared to patients treated with clopidogrel. There were no significant differences in bleeding for the prasugrel and clopidogrel arms of the trial. Prasugrel demonstrated a comparable safety profile to clopidogrel (Eli Lilly, Sankyo, AUG 2004). Three phase I trials showed that prasugrel prevented platelet aggregation better than clopidogrel, with less variability in terms of response rates and inhibition of platelet aggregation in prasugrel-treated patients. In a trial in 68 healthy subjects, a greater than 25% inhibition of platelet aggregation was achieved in all patients treated with a 60 mg loading dose of prasugrel compared with 42.4% of patients administered the approved 300 mg loading dose of clopidogrel. In a trial in 30 male volunteers administered once-daily maintenance doses of prasugrel (5, 10, or 20 mg), clopidogrel (75 mg), or placebo, the maximum level of platelet inhibition after ten days was greater for all prasugrel doses than with clopidogrel or placebo. In a trial in 101 aspirin-treated patients with stable atherosclerotic vascular disease, significantly higher levels of platelet inhibition were achieved in patients receiving 40 and 60 mg prasugrel loading doses compared with those on a 300 mg clopidogrel loading dose. After 28 days, higher levels of platelet inhibition were recorded in patients on prasugrel 10 and 15 mg maintenance doses compared with those on 75 mg clopidogrel. There was a trend towards more bruising and minor bleeding with the 15 mg prasugrel maintenance dose (Lilly, MAR 2005). Pooled results from three early-phase single-center trials in a total of 112 healthy volunteers (aged 18-65 years) randomized to loading doses of either 60 mg prasugrel or 300 mg clopidogrel in a two-way cross-over design showed that while all subjects responded to prasugrel not all of the same subjects responded to clopidogrel, according to objectively defined parameters for inhibition of platelet aggregation (IPA). ADP was used to induce platelet aggregation in samples of subjects' blood, and IPA and change in maximum platelet aggregation (MPA) from baseline were evaluated at 4-5 h and 24 h after drug administration. Nonresponders were defined as those achieving less than 25% IPA or a difference of less than 20% in MPA in response to 5 mcm ADP, and less than 20% IPA or a difference of less than 15% in MPA to 20 mcm ADP. While all subjects responded to prasugrel, 22% and 43% were nonresponders to clopidogrel according to IPA with 5 mcm and 20 mcm ADP respectively (Lilly, OCT 2005). In a phase Ib trial in which 81 aspirin-treated patients with stable cardiovascular disease were randomized to either the 300 mg approved loading dose of clopidogrel or 40 mg or 60 mg prasugrel, inhibition of platelet aggregation and change in maximum platelet aggregation from baseline were evaluated 6 h after drug administration. More than 90% of prasugrel patients compared with less than 50% of clopidogrel patients achieved greater than 20% inhibition of platelet aggregation. Even patients with more reactive platelets at baseline (which may be less affected or unaffected by thienopyridine therapies) had higher and more consistent inhibition of platelet aggregation following prasugrel. In a second study in which blood from nine healthy donors, pre- and post-aspirin therapy, was incubated with varying concentrations of active prasugrel metabolites (with ADP used to induce platelet activation and aggregation), rapid, potent and consistent inhibition of both platelet activation and generation of thrombo-inflammatory markers was achieved, independent of the effects of aspirin. Pre-treatment with aspirin did not appear to be required for prasugrel blockade of ADP-induced platelet activation (Lilly, MAR 2006).

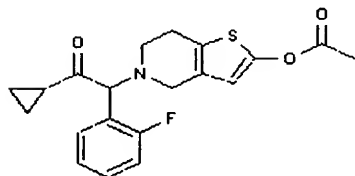
DEVELOPMENT HISTORY:

OCT 2005	Daiichi merged with Sankyo to form Daiichi Sankyo.
NOV 2004	Phase III, Worldwide (coronary artery disease).
JAN 2004	Phase II, USA, Europe (ischemia).
2003	Phase II, USA (coronary artery disease).

JUN 2002 Phase I, USA, Japan.
DEC 2000 Letter of intent signed between Sankyo and Lilly.
FEB 1998 Phase I, Europe.
SEP 1991 Priority product patent application filed in Japan, by Sankyo and Ube.

L53 ANSWER 30 OF 56 PROUSDDR COPYRIGHT 2006 PROUS SCIENCE on STN
ACCESSION NUMBER: 1999:3152 PROUSDDR
DOCUMENT NUMBER: 273686
CHEMICAL NAME: Acetic acid 5-(2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl)-4,5,6,7-tetrahydrothieno(3,2-c)pyridin-2-yl ester
DRUG NAME: CS-747
LY-640315
GENERIC NAME: Prasugrel (Prop INN, USAN)
CAS REGISTRY NUMBER: 150322-43-3
389574-19-0 (hydrochloride)
MOLECULAR FORMULA: C20 H20 F N O3 S
STATUS: Actively Investigated
HIGHEST DEV. PHASE: PHASE III
ORIGINATOR: Sankyo
Ube
LICENSEE: Lilly
CLASSIFICATION CODE: Antiplatelet Therapy
ACTION MECHANISM: P2Y12 (P2T) Antagonists
OTHER SOURCE: SYNTHLINE 2001001093; PROUSDDR 2001004790
(Metabolite); 343867 (Metabolite); 343880
(Metabolite); 349314 (Metabolite); 349316 (Metabolite)
ENTRY DATE: Entered STN: 9 May 2004
Last Updated on STN: 4 Aug 2006

STRUCTURE:



PROUS REFERENCES:

RefID: 527623 (Text Available)
Drug Data Report, Vol. 21, No. 4, pp 323, 1999
RefID: 636139
Drugs of the Future, Vol. 26, No. 9, pp 835, 2001

REFERENCE TEXT:

RefID: 527623
ACTION - Antiplatelet agent, a potent P2T purinoceptor antagonist. Phase I clinical trials in healthy volunteers demonstrated that a single oral dose of compound (30 or 75 mg) produced rapid (1 h) and long-lasting inhibition (> 48 h) of ex vivo ADP- but not collagen-induced platelet aggregation. In a multiple-dose study, 10 mg p.o. inhibited platelet aggregation for at least 2 days after treatment. Compound was devoid of serious side effects.

Potentially useful for the treatment or prevention of cardiovascular events such as unstable angina, myocardial infarction or stroke.

PATENT REFERENCES:

TITLE: Novel medicinal compositions of hydropyridines
INVENTOR(S): Ogawa, T.; Inoue, T.; Asai, F.
PATENT ASSIGNEE(S): Sankyo
PATENT ASSIGNEE(S): Ube
PATENT INFORMATION: JP 98310586 19981124
WO 9749397 19971231
PRIORITY INFORMATION: JP 1996-166126 19960626
JP 1997-54587 19970310

TITLE: 2-Silyloxytetrahydrothienopyridine, salt thereof and process for preparing the same
INVENTOR(S): Yamamoto, Y.; Miyata, H.; Ataka, K.; Kohno, M.; Yokota, N.
PATENT ASSIGNEE(S): Ube
PATENT INFORMATION: US 5874581 19990223
WO 9611203 19960418
PRIORITY INFORMATION: JP 1994-244141 19941007

TITLE: Hydropyridine derivative acid addition salts
INVENTOR(S): Nakamura, K.; Ogawa, T.; Inoue, T.; Asai, F.; Naganuma, H.; Yamamura, N.
PATENT ASSIGNEE(S): Sankyo
PATENT ASSIGNEE(S): Ube
PATENT INFORMATION: EP 1298132 20030402
JP 2002145883 20020522
US 2003134872 20030717
US 6693115 20040217
WO 2002004461 20020117
PRIORITY INFORMATION: JP 2000-205396 20000706
JP 2000-266780 20000904

TITLE: Medicinal compositions containing aspirin
INVENTOR(S): Ogawa, T.; Inoue, T.; Asai, F.; Sugidachi, A.
PATENT ASSIGNEE(S): Sankyo
PATENT ASSIGNEE(S): Ube
PATENT INFORMATION: JP 2002255814 20020911
WO 2002051412 20020704
PRIORITY INFORMATION: JP 2000-392983 20001225

TITLE: Medicines containing acid additive salts of hydropyridine derivatives
INVENTOR(S): Nakamura, K.; Ogawa, T.; Inoue, T.; Asai, F.; Naganuma, H.; Yamamura, N.
PATENT ASSIGNEE(S): Sankyo
PATENT ASSIGNEE(S): Ube
PATENT INFORMATION: JP 2003246735 20030902
PRIORITY INFORMATION: JP 2001-388757 20011221

TITLE: Medicinal composition for treating arteriosclerosis
INVENTOR(S): Ogawa, T.; Inaba, T.; Asai, F.
PATENT ASSIGNEE(S): Sankyo
PATENT INFORMATION: JP 2004051639 20040219
WO 2004009119 20040129
PRIORITY INFORMATION: JP 2002-209165 20020718

TITLE: Treating cardiovascular diseases with a compound of formula 1 (CS 747 - prasugrel; RN 150322-43-4)
INVENTOR(S): Jakubowski, J.A.; Farid, N.A.; Brandt, J.T.; Winters, K.J.
PATENT ASSIGNEE(S): Lilly
PATENT INFORMATION: EP 1660183 20060531
WO 2004098713 20041118
PRIORITY INFORMATION: US 2003-467903 20030505

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Hirota, T.; Sugii, H.; Asai, F.; Kawabata, K.; Inoue, T.; Iwamura, R.; Freestone, S.; Dickson, J., Annu Meet Am Soc Clin Pharmacol Ther (ASCPT) (100th Edition), March 18 1999-March 20 1999, San Antonio, (Abst PII-5)
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Asai, F.; Sugidachi, A.; Ogawa, T.; Nagasawa, T.; Shimoji, T.; Suzuki, N.; Kawamura, Y.; Inoue, T.; Iwamura, R., Thromb Haemost, No. Suppl., (Abst 2626), 1999
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"Pharmacokinetics and disposition of CS-747, a new pro-drug ADP-receptor antagonist, in rats and dogs"
Ikeda, T.; Iwabuchi, H.; Kawabata, K.; Tsutsumi, S.; Suzuki, N.; Sone, J.; Yoneda, K.; Kita, J., Thromb Haemost, No. Suppl., (Abst 2627), 1999
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Sugidachi, A.; Asai, F.; Ogawa, T.; Inoue, T.; Koike, H., Br J Pharmacol, Vol. 129, No. 7, pp 1439, 2000
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Sugidachi, A.; Asai, F.; Yoneda, K.; Iwamura, R.; Ogawa, T.; Otsuguro, K.; Koike, H., Br J Pharmacol, Vol. 132, No. 1, pp 47, 2001
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Otsuguro, K.; Asai, F.; Sugidachi, A.; Ogawa, T.; Nagasawa, T.; Shimoji, T.; Suzuki, N.; Fujisawa, Y.; Nakanishi, Y.; Inoue, T., Thromb Haemost, No. Suppl., (Abst P1901), 2001
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Asai, F.; Ogawa, T.; Sugidachi, A.; Otsuguro, K.; Shimoji, T.; Suzuki, N.; Fujisawa, Y.; Yoneda, K.; Iwamura, R., Thromb Haemost, No. Suppl., (Abst P1915), 2001
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Kazui, M.; et al., Xenobiotic Metab Dispos, Vol. 16, No. Suppl., (Abst 17S1-01), 2001
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Asai, F.; Niitsu, Y.; Ogawa, T.; et al., J Thromb Haemost, Vol. 1, No. Suppl. 1, (Abst P2033), 2003
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Sugidachi, A.; Ogawa, T.; Isobe, T.; Shimoji, T.; Suzuki, N.; Kakusaka, M.; Asai, F., J Thromb Haemost, Vol. 1, No. Suppl. 1, (Abst P2032), 2003
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Wallentin, L.; et al., Annu Sci Sess Am Coll Cardiol (ACC) (54th Edition), March 6 2005-March 9 2005, Orlando, (Abst 1126-136)
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Payne, C.D.; et al., Congr Int Soc Thromb Haemost (ISTH) (20th Edition), August 6 2005-August 12 2005, Sydney, (Abst P0952)
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Weerakkody, G.J.; Brandt, J.T.; Payne, C.D.; Jakubowski, J.A.; Farid, N.A.; Naganuma, H.; Winters, K.J., Am J Cardiol, Vol. 96, No. 7, Suppl. 1, (Abst TCT-32), 2005
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increased inhibition of platelet aggregation"

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ACCESSION NUMBER: 2006194112 EMBASE
TITLE: The Year in Interventional Cardiology.
AUTHOR: Dixon S.R.; Grines C.L.; O'Neill W.W.
CORPORATE SOURCE: Dr. W.W. O'Neill, William Beaumont Hospital, Royal Oak, MI, United States. woneill@beaumont.edu
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038 Adverse Reactions Titles

039 Pharmacy

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ABSTRACT: The Year in Interventional Cardiology. Simon R. Dixon, Cindy L. Grines, William W. O'Neill. .COPYRGT. 2006 American College of Cardiology Foundation.

CONTROLLED TERM: Medical Descriptors:

- *interventional cardiovascular procedure
- acute heart infarction: DT, drug therapy
- acute heart infarction: SU, surgery
- acute heart infarction: TH, therapy
- percutaneous coronary intervention
- blood clot lysis
- heart muscle revascularization
- heart failure
- coronary stent
- angioplasty
- ST segment elevation
- bleeding: SI, side effect
- drug safety
- low drug dose
- intermethod comparison
- stroke
- drug megadose
- thrombectomy
- heart catheterization
- stem cell transplantation
- nuclear magnetic resonance imaging
- heart ejection fraction
- cardiogenic shock: CO, complication
- acute coronary syndrome
- coronary artery disease: SU, surgery
- coronary artery disease: TH, therapy
- coronary artery bypass graft
- drug eluting stent
- treatment outcome
- heart muscle ischemia: TH, therapy
- restenosis: CO, complication
- restenosis: DM, disease management
- restenosis: DT, drug therapy
- restenosis: PC, prevention
- restenosis: RT, radiotherapy
- saphenous vein graft
- thrombosis: CO, complication
- cost effectiveness analysis
- brachytherapy
- artery intima proliferation: CO, complication
- biocompatibility
- balloon occlusion
- aorta disease: TH, therapy
- carotid artery disease: TH, therapy
- drug hypersensitivity: SI, side effect
- thrombocyte aggregation
- drug eruption: SI, side effect
- human
- clinical trial
- review

CONTROLLED TERM:

priority journal

Drug Descriptors:

tissue plasminogen activator: AE, adverse drug reaction

tissue plasminogen activator: CT, clinical trial

tissue plasminogen activator: DO, drug dose

tissue plasminogen activator: DT, drug therapy

reteplase: CT, clinical trial

reteplase: DT, drug therapy

tenecteplase: AE, adverse drug reaction

tenecteplase: CT, clinical trial

tenecteplase: DO, drug dose

tenecteplase: DT, drug therapy

clopidogrel: AE, adverse drug reaction

clopidogrel: CT, clinical trial

clopidogrel: CB, drug combination

clopidogrel: DT, drug therapy

clopidogrel: PD, pharmacology

heparin: CT, clinical trial

heparin: CM, drug comparison

heparin: DO, drug dose

heparin: DT, drug therapy

abciximab: AE, adverse drug reaction

abciximab: CT, clinical trial

abciximab: CB, drug combination

abciximab: DT, drug therapy

adenosine: CT, clinical trial

adenosine: DO, drug dose

adenosine: DT, drug therapy

adenosine: IV, intravenous drug administration

nicorandil: CT, clinical trial

nicorandil: DT, drug therapy

nicorandil: IV, intravenous drug administration

nicorandil: PD, pharmacology

granulocyte colony stimulating factor: CT, clinical trial

granulocyte colony stimulating factor: CB, drug combination

granulocyte colony stimulating factor: DT, drug therapy

granulocyte colony stimulating factor: IV, intravenous drug administration

granulocyte colony stimulating factor: PD, pharmacology

vasculotropin: AE, adverse drug reaction

vasculotropin: CT, clinical trial

vasculotropin: DT, drug therapy

vasculotropin: IM, intramuscular drug administration

vasculotropin: PD, pharmacology

plasmid DNA: AE, adverse drug reaction

plasmid DNA: CT, clinical trial

plasmid DNA: DT, drug therapy

plasmid DNA: IM, intramuscular drug administration

plasmid DNA: PD, pharmacology

monoclonal antibody cd 34: CT, clinical trial

monoclonal antibody cd 34: DT, drug therapy

monoclonal antibody: CT, clinical trial

monoclonal antibody: DT, drug therapy

rapamycin: CT, clinical trial

rapamycin: CM, drug comparison

rapamycin: DT, drug therapy

rapamycin: PR, pharmaceuticals

paclitaxel: CT, clinical trial

paclitaxel: CM, drug comparison

paclitaxel: DT, drug therapy

paclitaxel: PR, pharmaceuticals
 abt 578: CT, clinical trial
 abt 578: DT, drug therapy
 abt 578: PR, pharmaceuticals
 everolimus: CT, clinical trial
 everolimus: DT, drug therapy
 everolimus: PR, pharmaceuticals
 cilostazol: AE, adverse drug reaction
 cilostazol: CT, clinical trial
 cilostazol: CB, drug combination
 cilostazol: DT, drug therapy
 cilostazol: PO, oral drug administration
 cilostazol: PD, pharmacology
 pioglitazone: CT, clinical trial
 pioglitazone: DT, drug therapy
 pioglitazone: PO, oral drug administration
 pioglitazone: PD, pharmacology
 acetylsalicylic acid: AE, adverse drug reaction
 acetylsalicylic acid: CB, drug combination
 acetylsalicylic acid: DO, drug dose
 acetylsalicylic acid: DT, drug therapy
 ticlopidine: AE, adverse drug reaction
 ticlopidine: CT, clinical trial
 ticlopidine: CB, drug combination
 ticlopidine: DT, drug therapy
 prasugrel: AE, adverse drug reaction
 prasugrel: CT, clinical trial
 prasugrel: DT, drug therapy
 prasugrel: PD, pharmacology
 enoxaparin: CT, clinical trial
 enoxaparin: CB, drug combination
 enoxaparin: DT, drug therapy
 fondaparinux: AE, adverse drug reaction
 fondaparinux: CT, clinical trial
 fondaparinux: DT, drug therapy
 unclassified drug

CAS REGISTRY NO.: (tissue plasminogen activator) 105913-11-9; (reteplase) 133652-38-7; (tenecteplase) 191588-94-0; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (abciximab) 143653-53-6; (adenosine) 58-61-7; (nicorandil) 65141-46-0; (vasculotropin) 127464-60-2; (rapamycin) 53123-88-9; (paclitaxel) 33069-62-4; (everolimus) 159351-69-6; (cilostazol) 73963-72-1; (pioglitazone) 105355-27-9, 111025-46-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (ticlopidine) 53885-35-1, 55142-85-3; (prasugrel) 389574-19-0; (enoxaparin) 9041-08-1; (fondaparinux) 104993-28-4, 114870-03-0

NAME OF PRODUCT: (1) Cypher; (2) 'Taxus'; aspirin
 COMPANY NAME: Otsuka (United States); Takeda (Japan)
 COMPANY NAME: (1) Johnson and Johnson; (2) Boston Scientific; Medtronic (Italy) ; Sorin (United States) ; Kensey Nash (United States) ; St Jude

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ACCESSION NUMBER: 2006163293 EMBASE

TITLE: Clopidogrel treatment prior to **percutaneous coronary** intervention: When enough isn't enough.

AUTHOR: Steinhubl S.R.; Charnigo R.
CORPORATE SOURCE: Dr. S.R. Steinhubl, 326 Charles T. Wethington Bldg, 900 S
Limestone St, Lexington, KY 40536-0200, United States.
steinhubl@uky.edu
SOURCE: Journal of the American Medical Association, (5 Apr 2006)
Vol. 295, No. 13, pp. 1581-1582. .
Refs: 20
ISSN: 0098-7484 E-ISSN: 1538-3598 CODEN: JAMAAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 2006
Last Updated on STN: 25 Apr 2006
CONTROLLED TERM: Medical Descriptors:
*percutaneous coronary intervention
acute coronary syndrome: DT, drug therapy
acute coronary syndrome: SU, surgery
acute coronary syndrome: TH, therapy
unstable angina pectoris: DT, drug therapy
unstable angina pectoris: SU, surgery
unstable angina pectoris: TH, therapy
heart infarction: DT, drug therapy
heart infarction: SU, surgery
heart infarction: TH, therapy
Q wave
transluminal coronary angioplasty
drug activity
drug effect
risk reduction
thrombocyte aggregation inhibition
drug efficacy
treatment duration
revascularization
coronary stent
ST segment elevation
human
clinical trial
editorial
priority journal
CONTROLLED TERM: Drug Descriptors:
*clopidogrel: CT, clinical trial
*clopidogrel: DO, drug dose
*clopidogrel: DT, drug therapy
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
heparin: CT, clinical trial
heparin: CM, drug comparison
heparin: DT, drug therapy
heparin: PD, pharmacology
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: PD, pharmacology
abciximab: CT, clinical trial
abciximab: DT, drug therapy
abciximab: PD, pharmacology

eptifibatide: CT, clinical trial
eptifibatide: DT, drug therapy
eptifibatide: PD, pharmacology
tirofiban: CT, clinical trial
tirofiban: DT, drug therapy
ticlopidine: CT, clinical trial
ticlopidine: DT, drug therapy
troponin T: EC, endogenous compound
low molecular weight heparin: DT, drug therapy
antithrombocytic agent: DT, drug therapy
prasugrel: DT, drug therapy
cangrelor: DT, drug therapy
cangrelor: PA, parenteral drug administration
thrombin inhibitor: DT, drug therapy
azd 6140
sch 530348

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4,
94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2,
53663-74-4, 53664-49-6, 63781-77-1; (heparin) 37187-54-5,
8057-48-5, 8065-01-8, 9005-48-5; (abciximab) 143653-53-6;
(eptifibatide) 148031-34-9; (tirofiban) 142373-60-2,
144494-65-5, 150915-40-5; (ticlopidine) 53885-35-1,
55142-85-3; (troponin T) 60304-72-5; (prasugrel)
389574-19-0

CHEMICAL NAME: Azd 6140; Sch 530348

L53 ANSWER 33 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006163286 EMBASE

TITLE: Abciximab in patients with acute **coronary**
syndromes undergoing **percutaneous**
coronary intervention after clopidogrel
pretreatment: The ISAR-REACT 2 randomized trial.

AUTHOR: Kastrati A.; Mehilli J.; Neumann F.-J.; Dotzer F.; Ten Berg
J.; Bollwein H.; Graf I.; Ibrahim M.; Pache J.; Seyfarth
M.; Schuhlen H.; Dirschinger J.; Berger P.B.; Schomig A.

CORPORATE SOURCE: Dr. A. Kastrati, Deutsches Herzzentrum, Lazarettstrasse 36,
80636 Munich, Germany. kastrati@dhm.mhn.de

SOURCE: Journal of the American Medical Association, (5 Apr 2006)
Vol. 295, No. 13, pp. 1531-1538. .
Refs: 41

ISSN: 0098-7484 E-ISSN: 1538-3598 CODEN: JAMAAP

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 25 Apr 2006

Last Updated on STN: 25 Apr 2006

ABSTRACT: Context: No specifically designed studies have addressed the role of
the glycoprotein IIb/IIIa inhibitor abciximab in patients with non-ST-segment
elevation acute **coronary** syndromes (ACS) undergoing
percutaneous **coronary** intervention (PCI) after
pretreatment with 600 mg of clopidogrel. Objective: To assess whether
abciximab is associated with clinical benefit in highrisk patients with ACS
undergoing PCI after pretreatment with 600 mg of clopidogrel.
Design, Setting, and Patients: International, multicenter, randomized,

doubleblind, placebo-controlled study conducted from March 2003 through December 2005, enrolling 2022 patients (mean age, 66 years) with non-ST-segment elevation ACS undergoing PCI. Interventions: Patients were assigned to receive either abciximab (0.25 mg/kg of body weight bolus, followed by a 0.125-µg/kg per minute [maximum, 10 µg/min] infusion for 12 hours, plus heparin, 70 U/kg of body weight) or placebo (placebo bolus and infusion of 12 hours, plus heparin bolus, 140 U/kg). All patients received clopidogrel, 600 mg, at least 2 hours prior to the procedure, as well as 500 mg of oral or intravenous aspirin. Main Outcome Measures: The primary end point was a composite of death, myocardial infarction, or urgent target vessel revascularization occurring within 30 days after randomization; secondary end points were rates of in-hospital major and minor bleeding. Results: Of 2022 patients enrolled, 1012 were assigned to abciximab and 1010 to placebo. The primary end point was reached in 90 patients (8.9%) assigned to abciximab vs 120 patients (11.9%) assigned to placebo, a 25% reduction in risk with abciximab (relative risk [RR], 0.75; 95% CI, 0.58-0.97; P=.03). Among patients without an elevated troponin level, there was no difference in the incidence of primary end point events between the abciximab group (23/499 patients [4.6%]) and the placebo group (22/474 patients [4.6%]) (RR, 0.99; 95% CI, 0.56-1.76; P=.98), whereas among patients with an elevated troponin level, the incidence of events was significantly lower in the abciximab group (67/513 patients [13.1%]) compared with the placebo group (98/536 patients [18.3%]), which corresponds to an RR of 0.71 (95% CI, 0.54-0.95; P=.02) (P=.07 for interaction). There were no significant differences between the 2 groups regarding the risk of major and minor bleeding as well as need for transfusion. Conclusions: Abciximab reduces the risk of adverse events in patients with non-ST-segment elevation ACS undergoing PCI after pretreatment with 600 mg of clopidogrel. The benefits provided by abciximab appear to be confined to patients presenting with an elevated troponin level. .COPYRIGHT.2006 American Medical Association. All rights reserved.

CONTROLLED TERM: Medical Descriptors:
 *acute coronary syndrome: DT, drug therapy
 *acute coronary syndrome: TH, therapy
 percutaneous coronary intervention
ST segment elevation
drug effect
high risk patient
bolus injection
outcome assessment
treatment outcome
 heart death: SI, side effect
 heart infarction: SI, side effect
 revascularization: SI, side effect
bleeding: SI, side effect
hospitalization
risk reduction
incidence
drug efficacy
drug binding
electrocardiogram
drug safety
demography
thrombocytopenia: SI, side effect
human
male
female
major clinical study
clinical trial
randomized controlled trial

double blind procedure
multicenter study
controlled study
aged
adult
article
priority journal

CONTROLLED TERM: Drug Descriptors:
*abciximab: AE, adverse drug reaction
*abciximab: CT, clinical trial
*abciximab: AD, drug administration
*abciximab: CB, drug combination
*abciximab: DO, drug dose
*abciximab: DT, drug therapy
*abciximab: PD, pharmacology
*clopidogrel: DO, drug dose
*clopidogrel: DT, drug therapy
heparin: CT, clinical trial
heparin: CB, drug combination
heparin: DO, drug dose
heparin: DT, drug therapy
placebo
 acetylsalicylic acid: DO, drug dose
 acetylsalicylic acid: DT, drug therapy
 acetylsalicylic acid: IV, intravenous drug
administration
 acetylsalicylic acid: PO, oral drug administration
troponin: EC, endogenous compound
beta adrenergic receptor blocking agent: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
nitrate: DT, drug therapy
calcium antagonist: DT, drug therapy
prasugrel
cangrelor
azd 6140

CAS REGISTRY NO.: (abciximab) 143653-53-6; (clopidogrel) 113665-84-2,
120202-66-6, 90055-48-4, 94188-84-8; (heparin) 37187-54-5,
8057-48-5, 8065-01-8, 9005-48-5; (acetylsalicylic acid)
493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1;
(nitrate) 14797-55-8; (prasugrel) 389574-19-0

CHEMICAL NAME: Azd 6140

L53 ANSWER 34 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006345426 EMBASE

TITLE: Clopidogrel resistance: Implications for coronary stenting.

AUTHOR: Gurbel P.A.; Lau W.C.; Bliden K.P.; Tantry U.S.

CORPORATE SOURCE: P.A. Gurbel, Sinai Center for Thrombosis Research, 2401 W. Belvedere Ave., Baltimore, MD 21215, United States.
Pgurbel@lifebridgehealth.org

SOURCE: Current Pharmaceutical Design, (2006) Vol. 12, No. 10, pp. 1261-1269. .
Refs: 56
ISSN: 1381-6128 CODEN: CPDEFP

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology

036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 10 Aug 2006

Last Updated on STN: 10 Aug 2006

ABSTRACT: Clopidogrel, in combination with aspirin, is currently the drug of choice to prevent thrombosis after coronary stent implantation. Currently, clopidogrel is administered to the vast majority of patients without any assessment of platelet inhibition. Response variability and resistance, however, definitely occur to clopidogrel treatment. Preliminary data support the hypothesis that patients with reactive or clopidogrel nonresponsive platelets are at risk for thrombotic events. However, the magnitude of the clinical effect remains unknown and relationship between nonresponsiveness and risk of clinical events is under-investigated. Several important questions that must be answered are: A) What is the relation of clopidogrel resistance and high platelet reactivity to the occurrence of stent thrombosis, recurrent myocardial infarction, stroke and death?; B) Is there a threshold of platelet reactivity that correlates with the onset of thrombotic risk?; and C) What is the cost of administering clopidogrel to non-responsive patients? Finally, our understanding of the clinical relevance of drug resistance and high platelet reactivity should be facilitated by the use of validated point-of-service devices. The mechanisms of the response variability to clopidogrel remain incompletely defined. The contribution of intra- and extracellular pathways are under investigation. .COPYRIGHT. 2006 Bentham Science Publishers Ltd.

CONTROLLED TERM: Medical Descriptors:

- *coronary stent
- *coronary artery thrombosis: CO, complication
- *coronary artery thrombosis: DM, disease management
- *coronary artery thrombosis: DR, drug resistance
- *coronary artery thrombosis: DT, drug therapy
- *coronary artery thrombosis: PC, prevention
- drug choice
- drug efficacy
- cardiovascular risk
- thrombocyte function
- heart infarction
- recurrent disease
- cerebrovascular accident
- mortality
- drug cost
- dose response
- thrombocyte activation
- anticoagulation
- drug mechanism
- drug metabolism
- calcium cell level
- thrombocyte aggregation inhibition
- drug antagonism
- drug potentiation
- cardiotoxicity: SI, side effect
- acute coronary syndrome: DT, drug therapy
- high risk patient
- drug dose regimen
- maintenance drug dose
- breath analysis
- drug megadose
- protein function

protein phosphorylation
human
nonhuman
clinical trial
review
priority journal

CONTROLLED TERM:

Drug Descriptors:

*clopidogrel: AE, adverse drug reaction
*clopidogrel: CT, clinical trial
*clopidogrel: CB, drug combination
*clopidogrel: CM, drug comparison
*clopidogrel: DO, drug dose
*clopidogrel: IT, drug interaction
*clopidogrel: DT, drug therapy
*clopidogrel: PE, pharmacoeconomics
*clopidogrel: PK, pharmacokinetics
*clopidogrel: PD, pharmacology
 acetylsalicylic acid: CB, drug combination
 acetylsalicylic acid: DT, drug therapy
 acetylsalicylic acid: PD, pharmacology
adenosine diphosphate: EC, endogenous compound
thrombocyte receptor: EC, endogenous compound
purine P2Y12 receptor: EC, endogenous compound
purine P2Y1 receptor: EC, endogenous compound
fibrinogen receptor: EC, endogenous compound
calcium: EC, endogenous compound
prasugrel
atorvastatin: AE, adverse drug reaction
atorvastatin: CT, clinical trial
atorvastatin: CB, drug combination
atorvastatin: CM, drug comparison
atorvastatin: IT, drug interaction
atorvastatin: DT, drug therapy
atorvastatin: PK, pharmacokinetics
cytochrome P450 3A4: EC, endogenous compound
pravastatin: CB, drug combination
pravastatin: IT, drug interaction
pravastatin: PK, pharmacokinetics
erythromycin: CT, clinical trial
erythromycin: CB, drug combination
erythromycin: CM, drug comparison
erythromycin: DO, drug dose
erythromycin: IT, drug interaction
rifampicin: CT, clinical trial
rifampicin: CB, drug combination
rifampicin: CM, drug comparison
rifampicin: DO, drug dose
rifampicin: IT, drug interaction
antibiotic agent: CT, clinical trial
antibiotic agent: CB, drug combination
antibiotic agent: CM, drug comparison
antibiotic agent: DO, drug dose
antibiotic agent: IT, drug interaction
hydroxymethylglutaryl coenzyme A reductase inhibitor: AE, adverse drug reaction
hydroxymethylglutaryl coenzyme A reductase inhibitor: CT, clinical trial
hydroxymethylglutaryl coenzyme A reductase inhibitor: CB, drug combination
hydroxymethylglutaryl coenzyme A reductase inhibitor: CM,

drug comparison
hydroxymethylglutaryl coenzyme A reductase inhibitor: IT,
drug interaction
hydroxymethylglutaryl coenzyme A reductase inhibitor: DT,
drug therapy
hydroxymethylglutaryl coenzyme A reductase inhibitor: PK,
pharmacokinetics
heparin

fibrinogen receptor antagonist
troleandomycin: IT, drug interaction
troleandomycin: DT, drug therapy
troleandomycin: TO, drug toxicity

abciximab: CT, clinical trial
abciximab: IT, drug interaction

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4,
94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2,
53663-74-4, 53664-49-6, 63781-77-1; (adenosine diphosphate)
20398-34-9, 58-64-0; (calcium) 7440-70-2; (prasugrel)
389574-19-0; (atorvastatin) 134523-00-5,
134523-03-8; (cytochrome P450 3A4) 329736-03-0;
(pravastatin) 81131-74-0; (erythromycin) 114-07-8,
70536-18-4; (rifampicin) 13292-46-1; (heparin) 37187-54-5,
8057-48-5, 8065-01-8, 9005-48-5; (troleandomycin)
2751-09-9; (abciximab) 143653-53-6

CHEMICAL NAME: (1) Cs 747; Aspirin

COMPANY NAME: (1) Sankyo (Japan)

L53 ANSWER 35 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006240444 EMBASE

TITLE: Prasugrel achieves greater inhibition of platelet aggregation and a lower rate of non-responders compared with clopidogrel in aspirin-treated patients with stable coronary artery disease.

AUTHOR: Jernberg T.; Payne C.D.; Winters K.J.; Darstein C.; Brandt J.T.; Jakubowski J.A.; Naganuma H.; Siegbahn A.; Wallentin L.

CORPORATE SOURCE: L. Wallentin, Department of Medical Sciences, Cardiology and Uppsala Clinical Research Center, University Hospital, 751 85 Uppsala, Sweden. lars.wallentin@ucr.uu.se

SOURCE: European Heart Journal, (2006) Vol. 27, No. 10, pp. 1166-1173. .

Refs: 22

ISSN: 0195-668X E-ISSN: 1522-9645 CODEN: EHJODF

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 006 Internal Medicine

018 Cardiovascular Diseases and Cardiovascular Surgery

025 Hematology

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 19 Jun 2006

Last Updated on STN: 19 Jun 2006

ABSTRACT: Aims: This study was designed to compare the degree of inhibition of platelet aggregation (IPA) of prasugrel with that of clopidogrel in stable aspirin-treated patients with coronary artery disease (CAD). Methods and results Subjects (n = 101) were randomly assigned to the following loading dose (LD) (day 1)/ maintenance dose (MD) (days 2-28) combinations: prasugrel, 40

mg/5 mg; 40 mg/7.5 mg; 60 mg/10 mg; 60 mg/15 mg; or clopidogrel, 300 mg/75 mg. Turbidometric platelet aggregation was measured at multiple timepoints during the study. At 4 h after dosing, with 20 μ M ADP, both prasugrel LDs achieved significantly higher mean IPA levels (60.6% and 68.4 vs. 30.0%, respectively; all $P < 0.0001$) and lower percentage (3 vs. 52%, $P < 0.0001$) of pharmacodynamic non-responders (defined as IPA $< 20\%$) than clopidogrel. Prasugrel 10 and 15 mg MDs achieved consistently higher mean IPA than clopidogrel 75 mg at day 28 (all $P < 0.0001$). At pre-MD on day 28, there were no non-responders in the 10 and 15 mg prasugrel group, compared with 45% in the clopidogrel group ($P = 0.0007$). Conclusion: In this population, prasugrel (40-60 mg LD and 10-15 mg MD) achieves greater IPA and a lower proportion of pharmacodynamic non-responders compared with the approved clopidogrel dosing. .COPYRGT. The European Society of Cardiology 2006. All rights reserved.

CONTROLLED TERM: Medical Descriptors:
 *thrombocyte aggregation inhibition
 *coronary artery disease: DT, drug therapy
 maintenance drug dose
 turbidimetry
 skin bruising: SI, side effect
 bleeding: SI, side effect
 epistaxis: SI, side effect
 gingiva bleeding: SI, side effect
 hemoptysis: SI, side effect
 blister: SI, side effect
 wound: SI, side effect
 conjunctival hemorrhage: SI, side effect
 hematuria: SI, side effect
 human
 male
 female
 clinical trial
 randomized controlled trial
 single blind procedure
 multicenter study
 controlled study
 aged
 adult
 article
 priority journal

CONTROLLED TERM: Drug Descriptors:
 *clopidogrel: AE, adverse drug reaction
 *clopidogrel: CT, clinical trial
 *clopidogrel: CB, drug combination
 *clopidogrel: CM, drug comparison
 *clopidogrel: DO, drug dose
 *clopidogrel: DT, drug therapy
 *acetylsalicylic acid: CT, clinical trial
 *acetylsalicylic acid: CB, drug combination
 *acetylsalicylic acid: DT, drug therapy
 *prasugrel: AE, adverse drug reaction
 *prasugrel: CT, clinical trial
 *prasugrel: CB, drug combination
 *prasugrel: CM, drug comparison
 *prasugrel: DO, drug dose
 *prasugrel: DT, drug therapy
 CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (prasugrel) 389574-19-0

CHEMICAL NAME: (1) Ecotrin; (2) Plavix; Cs 747
COMPANY NAME: (1) Glaxo SmithKline; (2) Sanofi Synthelabo; Sankyo (Japan)

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ACCESSION NUMBER: 2006211534 EMBASE

TITLE: P2Y(12) receptor antagonists: A rapidly expanding group of antiplatelet agents.

AUTHOR: Cattaneo M.

CORPORATE SOURCE: M. Cattaneo, Unita di Ematologia e Trombosi, Ospedale San Paolo-Universita di Milano, Via di Rudini 8, 20142 Milano, Italy. marco.cattaneo@unimi.it

SOURCE: European Heart Journal, (2006) Vol. 27, No. 9, pp. 1010-1012. .

Refs: 10

ISSN: 0195-668X E-ISSN: 1522-9645 CODEN: EHJODF

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Editorial

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

ENTRY DATE: Entered STN: 31 May 2006

Last Updated on STN: 31 May 2006

CONTROLLED TERM: Medical Descriptors:

pharmacodynamics

drug safety

thrombocyte aggregation inhibition

ischemic heart disease: DT, drug therapy

bleeding: SI, side effect

dyspnea: SI, side effect

human

clinical trial

editorial

priority journal

CONTROLLED TERM: Drug Descriptors:

*purine P2Y12 receptor: EC, endogenous compound

*purinergic receptor blocking agent: AE, adverse drug reaction

*purinergic receptor blocking agent: CT, clinical trial

*purinergic receptor blocking agent: CB, drug combination

*purinergic receptor blocking agent: CM, drug comparison

*purinergic receptor blocking agent: DO, drug dose

*purinergic receptor blocking agent: DT, drug therapy

*purinergic receptor blocking agent: PD, pharmacology

*purinergic receptor blocking agent: IV, intravenous drug administration

*purinergic receptor blocking agent: PO, oral drug administration

*purine P2Y12 receptor antagonist: AE, adverse drug reaction

*purine P2Y12 receptor antagonist: CT, clinical trial

*purine P2Y12 receptor antagonist: CB, drug combination

*purine P2Y12 receptor antagonist: CM, drug comparison

*purine P2Y12 receptor antagonist: DO, drug dose

*purine P2Y12 receptor antagonist: DT, drug therapy

*purine P2Y12 receptor antagonist: PD, pharmacology

*purine P2Y12 receptor antagonist: IV, intravenous drug administration

*purine P2Y12 receptor antagonist: PO, oral drug

administration

*antithrombocytic agent: AE, adverse drug reaction

*antithrombocytic agent: CT, clinical trial

*antithrombocytic agent: CB, drug combination

*antithrombocytic agent: CM, drug comparison

*antithrombocytic agent: DO, drug dose

*antithrombocytic agent: DT, drug therapy

*antithrombocytic agent: PD, pharmacology

*antithrombocytic agent: IV, intravenous drug

administration

*antithrombocytic agent: PO, oral drug administration

acetylsalicylic acid: CT, clinical trial

acetylsalicylic acid: CB, drug combination

acetylsalicylic acid: CM, drug comparison

acetylsalicylic acid: DT, drug therapy

acetylsalicylic acid: PD, pharmacology

acetylsalicylic acid: PO, oral drug administration

clopidogrel: CT, clinical trial

clopidogrel: CB, drug combination

clopidogrel: CM, drug comparison

clopidogrel: DT, drug therapy

clopidogrel: PD, pharmacology

clopidogrel: PO, oral drug administration

ticlopidine: CB, drug combination

ticlopidine: DT, drug therapy

ticlopidine: PD, pharmacology

prasugrel: CT, clinical trial

prasugrel: CM, drug comparison

prasugrel: DT, drug therapy

prasugrel: PD, pharmacology

cangrelor: CM, drug comparison

cangrelor: DT, drug therapy

cangrelor: PD, pharmacology

cangrelor: IV, intravenous drug administration

arc 109318xx: DT, drug therapy

arc 109318xx: PD, pharmacology

arc 109318xx: PO, oral drug administration

azd 6140: AE, adverse drug reaction

azd 6140: CT, clinical trial

azd 6140: CB, drug combination

azd 6140: CM, drug comparison

azd 6140: DO, drug dose

azd 6140: DT, drug therapy

azd 6140: PD, pharmacology

azd 6140: PO, oral drug administration

unclassified drug

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (ticlopidine) 53885-35-1, 55142-85-3; (prasugrel) 389574-19-0

CHEMICAL NAME: Azd 6140; Arc 109318xx

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ACCESSION NUMBER: 2006283984 EMBASE

TITLE: Rebound platelet activation after termination of prasugrel and aspirin therapy due to confirmed non-compliance in patient enrolled in the JUMBO Trial.

AUTHOR: Serebruany V.L.; Midei M.G.; Meilman H.; Malinin A.I.; Lowry D.R.

CORPORATE SOURCE: V.L. Serebruany, HeartDrug Research Laboratories, Osler Medical Center, 7600 Osler Drive, Towson, MD 21204, United States. heartdrug@aol.com

SOURCE: International Journal of Clinical Practice, (2006) Vol. 60, No. 7, pp. 863-866. .

Refs: 16

ISSN: 1368-5031 E-ISSN: 1742-1241 CODEN: IJCPF

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 14 Jul 2006

Last Updated on STN: 14 Jul 2006

ABSTRACT: Therapy with aspirin and/or adenosine diphosphate (ADP) receptor blockers is associated with better outcomes via inhibition of platelet activity, and subsequent reduction of ischemic vascular events. Non-compliance (NC) is a well-recognised hazard limiting the clinical utility of antiplatelet agents, and, probably worsening outcomes. However, comprehensive platelet characteristics of a confirmed NC patient after acute vascular event have never been reported within a major randomised trial with ADP-receptor antagonists. A 48-year-old male patient, well-educated, was among patients enrolled in the platelet sub-study for the JUMBO trial. He received 325 mg of aspirin daily for 9 months, presented with unstable angina for urgent coronary intervention, and was successfully reperfused with two intracoronary stents. The patient was randomised to a 60 mg prasugrel loading dose, and 10 mg of prasugrel daily for 30 days. Platelets were assessed at baseline, 4 and 24 h, and at 30 days after acute coronary event utilising ADP-, and collagen-induced conventional aggregometry, rapid cartridge-based analyser and flow cytometry. Loading with prasugrel resulted in significant inhibition of platelet activity during and after stenting. However, after assessing platelet biomarkers at 30 days, voluntary withdrawal from the antiplatelet agents was suspected. Based on the platelet activity characteristics, NC was later confirmed, and the patient admitted that he stopped taking both prasugrel and aspirin shortly after discharge due to minor bleeding episodes after shaving. Major platelet activity biomarkers of the index NC patient were compared with those from compliant prasugrel-, clopidogrel-treated patients, and healthy controls. The platelet tests uniformly revealed rebound activation by all platelet measures (at least twofold increase) while being especially high for ADP-, and collagen-induced aggregation, platelet/endothelial cell adhesion molecule-1 (PECAM-1), glycoprotein (GP)Ib, GPIIb/IIIa activity, P-selectin, protease activated receptor (PAR)-1 thrombin receptor (activated and intact epitopes), and thrombospondin expression. The clinical benefits of antiplatelet agents are not only denied in NC outpatients, but may put them at additional risk for worsened vascular outcomes due to the rebound platelet activation. Proclaimed 'resistance' to antiplatelet agents may at least in part be a result of NC, especially in the chronic uncontrolled setting. Enforcing compliance will improve outcomes in the clinical trials, and save lives of patients really receiving antiplatelet therapy. .COPYRGT. 2006 The Authors Journal compilation .COPYRGT. 2006 Blackwell Publishing Ltd.

CONTROLLED TERM: Medical Descriptors:

- *coronary artery disease: DT, drug therapy
- *coronary artery disease: PC, prevention
- thrombocyte activation
- drug withdrawal
- patient compliance
- drug dose regimen

unstable angina pectoris

flow cytometry

stent

hospital admission

hospital discharge

bleeding: SI, side effect

rebound

protein function

protein expression

human

male

case report

adult

article

priority journal

CONTROLLED TERM:

Drug Descriptors:

*prasugrel: AE, adverse drug reaction

*prasugrel: DO, drug dose

*prasugrel: DT, drug therapy

*acetylsalicylic acid: AE, adverse drug reaction

*acetylsalicylic acid: DO, drug dose

*acetylsalicylic acid: DT, drug therapy

adenosine diphosphate

collagen

antithrombocytic agent: AE, adverse drug reaction

antithrombocytic agent: DO, drug dose

antithrombocytic agent: DT, drug therapy

clopidogrel: DT, drug therapy

biological marker: EC, endogenous compound

CD31 antigen: EC, endogenous compound

glycoprotein Ib: EC, endogenous compound

fibrinogen receptor: EC, endogenous compound

PADGEM protein: EC, endogenous compound

proteinase activated receptor 1: EC, endogenous compound

thrombin receptor: EC, endogenous compound

thrombospondin: EC, endogenous compound

heparin: DT, drug therapy

eptifibatide: DT, drug therapy

metoprolol: DT, drug therapy

atorvastatin: DT, drug therapy

CAS REGISTRY NO.:

(prasugrel) 389574-19-0; (acetylsalicylic acid)

493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1;

(adenosine diphosphate) 20398-34-9, 58-64-0; (collagen)

9007-34-5; (clopidogrel) 113665-84-2, 120202-66-6,

90055-48-4, 94188-84-8; (heparin) 37187-54-5, 8057-48-5,

8065-01-8, 9005-48-5; (eptifibatide) 148031-34-9;

(metoprolol) 37350-58-6; (atorvastatin) 134523-00-5,

134523-03-8

CHEMICAL NAME:

Aspirin

L53 ANSWER 38 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006186415 EMBASE

TITLE: The platelet ATP and ADP receptors.

AUTHOR: Oury C.; Toth-Zsamboki E.; Vermynen J.; Hoylaerts M.F.

CORPORATE SOURCE: M.F. Hoylaerts, Center for Molecular and Vascular Biology, University of Leuven, Herestraat 49, B-3000 Leuven, Belgium. marc.hoylaerts@med.kuleuven.ac.be

SOURCE: Current Pharmaceutical Design, (2006) Vol. 12, No. 7, pp. 859-875. .

Refs: 156
ISSN: 1381-6128 CODEN: CPDEFP
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 May 2006
Last Updated on STN: 9 May 2006

ABSTRACT: Adenine nucleotides, ADP and ATP, are coreleased from dense granules during platelet activation, as well as from endothelial cells and damaged red blood cells following vascular injury. Through autocrine and paracrine mechanisms, these extracellular signaling molecules interact with the platelet P2 receptors to amplify ongoing platelet activation. Two receptors for ADP, the G(q)-protein-coupled P2Y(1) and G(i)-protein-coupled P2Y(12) and one receptor for ATP, the P2X(1) ion channel, have been identified on platelets. Due to distinct pharmacological properties and differential regulation, the P2Y and P2X receptors essentially operate on different scales of time and distance and trigger selective intracellular signaling cascades. Recent advances in the understanding of the P2Y receptor physiology have reinforced the concept of these receptors as useful targets for antithrombotic therapy. The function of P2X(1) in platelet activation only recently started to be unraveled. This review focuses on recent findings on the physiology of these platelet ADP and ATP receptors, their distinct downstream intracellular signaling pathways as well as on the available agonists, antagonists and inhibitors that allow their pharmacological discrimination. .COPYRGT. 2006 Bentham Science Publishers Ltd.

CONTROLLED TERM: Medical Descriptors:
protein secretion
thrombocyte activation
endothelium cell
blood vessel injury
signal transduction
hemostasis
thrombosis
protein analysis
protein function
protein localization
artery thrombosis: DT, drug therapy
artery thrombosis: PC, prevention
thrombocyte aggregation inhibition
neutropenia: SI, side effect
thrombocytopenic purpura: SI, side effect
human
nonhuman
review
priority journal

CONTROLLED TERM: Drug Descriptors:
*thrombocyte receptor: EC, endogenous compound
*adenosine triphosphate: EC, endogenous compound
*adenosine diphosphate: EC, endogenous compound
G protein coupled receptor: EC, endogenous compound
purine P2Y12 receptor: EC, endogenous compound
purine P2Y1 receptor: EC, endogenous compound
purine P2X1 receptor: EC, endogenous compound
purine P2X receptor: EC, endogenous compound

purine P2Y receptor: EC, endogenous compound
 anticoagulant agent
 purine receptor: EC, endogenous compound
 ticlopidine: AE, adverse drug reaction
 ticlopidine: CM, drug comparison
 ticlopidine: DT, drug therapy
 ticlopidine: PD, pharmacology
 clopidogrel: AE, adverse drug reaction
 clopidogrel: CB, drug combination
 clopidogrel: CM, drug comparison
 clopidogrel: DT, drug therapy
 clopidogrel: PD, pharmacology
 cangrelor
 prasugrel: PD, pharmacology
 2' deoxy 6 n methyladenosine 3',5' bisphosphate: AN, drug analysis
 2' deoxy 6 n methyladenosine 3',5' bisphosphate: DV, drug development
 2' deoxy 6 n methyladenosine 3',5' bisphosphate: PD, pharmacology
 purinergic receptor blocking agent: AN, drug analysis
 purinergic receptor blocking agent: DV, drug development
 purinergic receptor blocking agent: PD, pharmacology
 2 chloro 6 n methylmethanocarba 2' deoxyadenosine 3',5' bisphosphate: AN, drug analysis
 2 chloro 6 n methylmethanocarba 2' deoxyadenosine 3',5' bisphosphate: DV, drug development
 2 chloro 6 n methylmethanocarba 2' deoxyadenosine 3',5' bisphosphate: PD, pharmacology
 2 propylthio beta gamma dichloromethyleneadenosine triphosphate: AN, drug analysis
 2 propylthio beta gamma dichloromethyleneadenosine triphosphate: DV, drug development
 2 propylthio beta gamma dichloromethyleneadenosine triphosphate: PD, pharmacology
 acetylsalicylic acid: CB, drug combination
 acetylsalicylic acid: DT, drug therapy
 pyridoxal phosphate 6 azophenyl 2',4' disulfonic acid: PD, pharmacology
 suramin: AN, drug analysis
 suramin: DV, drug development
 4,4',4'',4''' (carbonylbis(imino 5,1,3 benzenetriylbis(carbonylimino)))tetrakis benzen 1,3 disulfonic acid: AN, drug analysis
 4,4',4'',4''' (carbonylbis(imino 5,1,3 benzenetriylbis(carbonylimino)))tetrakis benzen 1,3 disulfonic acid: DV, drug development
 4,4',4'',4''' (carbonylbis(imino 5,1,3 benzenetriylbis(carbonylimino)))tetrakis benzen 1,3 disulfonic acid: PD, pharmacology
 unclassified drug
 mrs 2279
 ar c67085mx
 nf 449
 CAS REGISTRY NO.: (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5;
 (adenosine diphosphate) 20398-34-9, 58-64-0; (ticlopidine) 53885-35-1, 55142-85-3; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (prasugrel) 389574-19-0; (2' deoxy 6 n methyladenosine 3',5' bisphosphate) 101204-49-3; (acetylsalicylic acid) 493-53-8,

50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (pyridoxal phosphate 6 azophenyl 2',4' disulfonic acid) 149017-66-3; (suramin) 129-46-4, 145-63-1

CHEMICAL NAME: Ar c69931mx; Cs 747; Plavix; Sr 25990c; Mrs 2179; Mrs 2279; Ar c67085mx; Aspirin; Nf 449

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ACCESSION NUMBER: 2006125569 EMBASE

TITLE: Aspirin and clopidogrel resistance: An emerging clinical entity.

AUTHOR: Wang T.H.; Bhatt D.L.; Topol E.J.

CORPORATE SOURCE: D.L. Bhatt, Department of Cardiovascular Medicine, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, United States. bhattd@ccf.org

SOURCE: European Heart Journal, (2006) Vol. 27, No. 6, pp. 647-654.

Refs: 98

ISSN: 0195-668X E-ISSN: 1522-9645 CODEN: EHJODF

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 28 Mar 2006

Last Updated on STN: 28 Mar 2006

ABSTRACT: Antiplatelet therapy is a cornerstone of cardiovascular medicine. Aspirin and clopidogrel have emerged as critical therapies in the treatment of cardiovascular disease. Despite their efficacy, patients on these medications continue to suffer complications. Millions of patients are currently on low-dose antiplatelet therapy but it is unknown how many of these patients are under-treated or on the wrong medication. Aspirin and clopidogrel resistance are emerging clinical entities with potentially severe consequences such as recurrent myocardial infarction, stroke, or death. The mechanism of resistance remains incompletely defined, but there are specific clinical, cellular, and genetic factors that influence therapeutic failure. These factors range from physicians who fail to prescribe these medications despite appropriate indications to polymorphisms of platelet membrane glycoproteins. Rapid and accurate diagnosis of anti-platelet resistance also remains an issue as new bedside tests are developed. By understanding the mechanism of therapeutic failure and by improving the diagnosis of this clinical entity, a new era of individualized antiplatelet therapy may arise with routine measurements of platelet activity in the same way that cholesterol, blood pressure, and blood sugar are followed, thus improving the care for millions of people. .COPYRGT. The European Society of Cardiology 2005. All rights reserved.

CONTROLLED TERM: Medical Descriptors:

*cardiovascular disease: DR, drug resistance
*cardiovascular disease: DT, drug therapy
*cardiovascular disease: PC, prevention
anticoagulant therapy
heart muscle ischemia: DR, drug resistance
heart muscle ischemia: DT, drug therapy
intracardiac thrombosis: DR, drug resistance
intracardiac thrombosis: DT, drug therapy
acute coronary syndrome: DR, drug resistance
acute coronary syndrome: DT, drug therapy

anticoagulation
 blood clot lysis
 risk reduction
 heart infarction: DR, drug resistance
 heart infarction: DT, drug therapy
 heart infarction: PC, prevention
 recurrent disease: DR, drug resistance
 recurrent disease: DT, drug therapy
 recurrent disease: PC, prevention
 ST segment elevation
 stroke: DT, drug therapy
 stroke: PC, prevention
 coronary artery thrombosis: DT, drug therapy
 coronary artery thrombosis: PC, prevention
 cardiovascular risk
 risk assessment
 age distribution
 secondary prevention
 heart protection
 drug treatment failure
 drug mechanism
 thrombocyte aggregation inhibition
 blood pressure
 glucose blood level
 cholesterol blood level
 monotherapy
 drug absorption
 patient compliance
 drug protein binding
 congestive heart failure: DT, drug therapy
 disease association
 hypercholesterolemia
 hyperglycemia
 drug efficacy
 pharmacogenetics
 drug megadose
 thrombocyte activation
 diagnostic test
 thrombocyte function
 high risk patient
 preventive medicine
 muscle necrosis: DT, drug therapy
 muscle necrosis: PC, prevention
 muscle necrosis: SU, surgery
 percutaneous coronary intervention
 bleeding: SI, side effect
 human
 clinical trial
 review
 priority journal

CONTROLLED TERM:

Drug Descriptors:
 *acetylsalicylic acid: AE, adverse drug reaction
 *acetylsalicylic acid: CT, clinical trial
 *acetylsalicylic acid: CM, drug comparison
 *acetylsalicylic acid: DO, drug dose
 *acetylsalicylic acid: IT, drug interaction
 *acetylsalicylic acid: DT, drug therapy
 *acetylsalicylic acid: PK, pharmacokinetics
 *acetylsalicylic acid: PD, pharmacology
 *clopidogrel: AE, adverse drug reaction

*clopidogrel: CT, clinical trial
*clopidogrel: CM, drug comparison
*clopidogrel: DO, drug dose
*clopidogrel: IT, drug interaction
*clopidogrel: DT, drug therapy
*clopidogrel: PK, pharmacokinetics
*clopidogrel: PD, pharmacology
antithrombocytic agent: AE, adverse drug reaction
antithrombocytic agent: CT, clinical trial
antithrombocytic agent: CM, drug comparison
antithrombocytic agent: DO, drug dose
antithrombocytic agent: IT, drug interaction
antithrombocytic agent: DT, drug therapy
antithrombocytic agent: PK, pharmacokinetics
antithrombocytic agent: PD, pharmacology
cholesterol: EC, endogenous compound
glucose: EC, endogenous compound
cyclooxygenase 1: EC, endogenous compound
cyclooxygenase 2: EC, endogenous compound
thromboxane b2 receptor: EC, endogenous compound
thromboxane receptor: EC, endogenous compound
cytochrome P450 3A4: EC, endogenous compound
atorvastatin
hydroxymethylglutaryl coenzyme A reductase inhibitor
adenosine diphosphate: EC, endogenous compound
pyridine derivative: CT, clinical trial
pyridine derivative: DT, drug therapy
pyridine derivative: PD, pharmacology
prasugrel: CT, clinical trial
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
azd 6140: CT, clinical trial
azd 6140: CM, drug comparison
azd 6140: DO, drug dose
azd 6140: DT, drug therapy
azd 6140: PO, oral drug administration
azd 6140: PK, pharmacokinetics
azd 6140: PD, pharmacology
purinergic receptor blocking agent: CT, clinical trial
purinergic receptor blocking agent: CM, drug comparison
purinergic receptor blocking agent: DO, drug dose
purinergic receptor blocking agent: DT, drug therapy
purinergic receptor blocking agent: PO, oral drug administration
purinergic receptor blocking agent: PK, pharmacokinetics
purinergic receptor blocking agent: PD, pharmacology
cangrelor: CM, drug comparison
cangrelor: DT, drug therapy
cangrelor: PK, pharmacokinetics
cangrelor: PD, pharmacology
thromboxane receptor blocking agent: AE, adverse drug reaction
thromboxane receptor blocking agent: CT, clinical trial
thromboxane receptor blocking agent: CM, drug comparison
thromboxane receptor blocking agent: DO, drug dose
thromboxane receptor blocking agent: IT, drug interaction
thromboxane receptor blocking agent: DT, drug therapy
thromboxane receptor blocking agent: PK, pharmacokinetics
thromboxane receptor blocking agent: PD, pharmacology
placebo

unclassified drug
CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4,
53664-49-6, 63781-77-1; (clopidogrel) 113665-84-2,
120202-66-6, 90055-48-4, 94188-84-8; (cholesterol) 57-88-5;
(glucose) 50-99-7, 84778-64-3; (cytochrome P450 3A4)
329736-03-0; (atorvastatin) 134523-00-5, 134523-03-8;
(adenosine diphosphate) 20398-34-9, 58-64-0; (prasugrel)
389574-19-0
CHEMICAL NAME: Aspirin; Cs 747; Ly 640315; Azd 6140

L53 ANSWER 40 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006186052 EMBASE
TITLE: Variable therapeutic effectiveness of clopidogrel in acute coronary syndromes.
AUTHOR: Hepstinstall S.
CORPORATE SOURCE: S. Heptinstall, Cardiovascular Medicine, University of Hospital, Queens Medical Centre, Nottingham NG7 2UH, United Kingdom. s.heptinstall@nottingham.ac.uk
SOURCE: Journal of Thrombosis and Haemostasis, (2006) Vol. 4, No. 3, pp. 539-541. .
Refs: 36
ISSN: 1538-7933 E-ISSN: 1538-7836 CODEN: JTHOA5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 8 May 2006
Last Updated on STN: 8 May 2006
CONTROLLED TERM: Medical Descriptors:
*acute coronary syndrome: DT, drug therapy
*acute coronary syndrome: SU, surgery
drug efficacy
percutaneous coronary intervention
coronary stent
clinical protocol
thrombocyte aggregation
follow up
heart muscle ischemia
thrombosis: CO, complication
thrombosis: DT, drug therapy
thrombosis: PC, prevention
risk assessment
drug dose regimen
drug metabolism
thrombocyte function
maintenance drug dose
human
clinical trial
note
priority journal
CONTROLLED TERM: Drug Descriptors:
*clopidogrel: CT, clinical trial
*clopidogrel: CM, drug comparison
*clopidogrel: DO, drug dose
*clopidogrel: DT, drug therapy
*clopidogrel: PK, pharmacokinetics

acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: DO, drug dose
acetylsalicylic acid: DT, drug therapy
ticlopidine: DT, drug therapy
hydroxymethylglutaryl coenzyme A reductase inhibitor
fibrinogen receptor antagonist: DT, drug therapy
prasugrel: CM, drug comparison
prasugrel: DT, drug therapy
prasugrel: PK, pharmacokinetics
cangrelor: DV, drug development
CAS REGISTRY NO.: (ticlopidine) 113665-84-2, 120202-66-6, 90055-48-4,
94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2,
53663-74-4, 53664-49-6, 63781-77-1; (ticlopidine)
53885-35-1, 55142-85-3; (prasugrel) 389574-19-0
CHEMICAL NAME: Aspirin
L53 ANSWER 41 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights
reserved on STN
ACCESSION NUMBER: 2006186051 EMBASE
TITLE: High postclopidogrel platelet reactivity in
non-ST-elevation acute coronary syndrome treated with
stenting: A clue for adverse prognosis?
AUTHOR: Galvani M.
CORPORATE SOURCE: M. Galvani, Fondazione Cardiologica Sacco, Ospedale
Morgagni, Cardiovascular Research Unit, P.zza F.lli Ruffini
6, 47100 Forli, Italy. galvanim@tin.it
SOURCE: Journal of Thrombosis and Haemostasis, (2006) Vol. 4, No.
3, pp. 536-538. .
Refs: 20
ISSN: 1538-7933 E-ISSN: 1538-7836 CODEN: JTHOA5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 006 Internal Medicine
017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 8 May 2006
Last Updated on STN: 8 May 2006
CONTROLLED TERM: Medical Descriptors:
*ST segment elevation
*thrombocyte activation
*acute coronary syndrome: DT, drug therapy
*acute coronary syndrome: SU, surgery
*postoperative thrombosis: CO, complication
*postoperative thrombosis: DT, drug therapy
*postoperative thrombosis: PC, prevention
coronary artery thrombosis: CO, complication
coronary artery thrombosis: DT, drug therapy
coronary artery thrombosis: PC, prevention
anticoagulant therapy
prognosis
coronary stent
coronary artery recanalization
percutaneous coronary intervention
high risk patient
blood sampling
thrombocyte aggregation
recurrent disease: CO, complication

stroke: CO, complication
surgical mortality
thrombocyte aggregation inhibition
reference value
elective surgery
evidence based medicine
human
note
priority journal

CONTROLLED TERM: Drug Descriptors:
*clopidogrel: CB, drug combination
*clopidogrel: CM, drug comparison
*clopidogrel: DT, drug therapy
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: DT, drug therapy
fibrinogen receptor antagonist: DT, drug therapy
tirofiban: DT, drug therapy
prasugrel: CM, drug comparison
prasugrel: DT, drug therapy

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4,
94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2,
53663-74-4, 53664-49-6, 63781-77-1; (tirofiban)
142373-60-2, 144494-65-5, 150915-40-5; (prasugrel)
389574-19-0

CHEMICAL NAME: Aspirin

L53 ANSWER 42 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006169266 EMBASE

TITLE: Aspirin and clopidogrel resistance.

AUTHOR: Michos E.D.; Ardehali R.; Blumenthal R.S.; Lange R.A.; Ardehali H.

CORPORATE SOURCE: Dr. H. Ardehali, Feinberg Cardiovascular Research Institute, Northwestern University Medical Center, Tarry 12-703, 303 East Chicago Ave, Chicago, IL 60611, United States. h-ardehali@northwestern.edu

SOURCE: Mayo Clinic Proceedings, (2006) Vol. 81, No. 4, pp. 518-526. .
Refs: 77
ISSN: 0025-6196 CODEN: MACPAJ

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 1 May 2006
Last Updated on STN: 1 May 2006

ABSTRACT: Despite aspirin's and clopidogrel's proven benefit in reducing cardiovascular (CV) events, recurrent CV events still occur in patients receiving antiplatelet therapy. Many of these patients are resistant or only partially responsive to the antiplatelet effects of aspirin and clopidogrel, as determined by standard platelet assays. However, current clinical guidelines do not support routine screening for aspirin or clopidogrel resistance, in part because determination of the most appropriate screening test has not been established. This review attempts to (1) describe the phenomena of clinical aspirin and clopidogrel resistance (ie, treatment failure), (2) discuss the complexity of defining and identifying aspirin and clopidogrel resistance, (3) identify factors that may be responsible for aspirin and clopidogrel resistance, (4) outline several standard platelet function assays and their

limitations, and (5) describe potential new antiplatelet therapies that may benefit aspirin- or clopidogrel-resistant patients. .COPYRGT. 2006 Mayo Foundation for Medical Education and Research.

CONTROLLED TERM: Medical Descriptors:

*cardiovascular disease: ET, etiology
 *thrombosis: DR, drug resistance
 *thrombosis: DT, drug therapy
 recurrent disease
 thrombocyte count
 practice guideline
 screening test
 vascular disease: DR, drug resistance
 vascular disease: DT, drug therapy
 human
 clinical trial
 meta analysis
 systematic review
 review

CONTROLLED TERM: Drug Descriptors:

*acetylsalicylic acid: DT, drug therapy
 *acetylsalicylic acid: PD, pharmacology
 *clopidogrel: IT, drug interaction
 *clopidogrel: DT, drug therapy
 *clopidogrel: PD, pharmacology
 *antithrombotic agent: DT, drug therapy
 *antithrombotic agent: PD, pharmacology
 *thieno[2,3 b]pyridine derivative: DT, drug therapy
 *thieno[2,3 b]pyridine derivative: PD, pharmacology
 cyclooxygenase 2: EC, endogenous compound
 purine P2Y receptor: EC, endogenous compound
 adenosine diphosphate: EC, endogenous compound
 metoprolol: DT, drug therapy
 rifampicin: IT, drug interaction
 rifampicin: DT, drug therapy
 cilostazol: CT, clinical trial
 cilostazol: DT, drug therapy
 cilostazol: PD, pharmacology
 prasugrel: CT, clinical trial
 prasugrel: DT, drug therapy
 prasugrel: PD, pharmacology
 bm 573: CT, clinical trial
 bm 573: DT, drug therapy
 bm 573: PD, pharmacology
 timi 38: CT, clinical trial
 timi 38: DT, drug therapy
 timi 38: PD, pharmacology
 purinergic receptor blocking agent: CT, clinical trial
 purinergic receptor blocking agent: DT, drug therapy
 purinergic receptor blocking agent: PD, pharmacology
 ar 69931mx: CT, clinical trial
 ar 69931mx: DT, drug therapy
 ar 69931mx: PD, pharmacology
 unclassified drug

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (adenosine diphosphate) 20398-34-9, 58-64-0; (metoprolol) 37350-58-6; (rifampicin) 13292-46-1; (cilostazol) 73963-72-1; (prasugrel) 389574-19-0

CHEMICAL NAME: Aspirin; Bm 573; Cs 747; Timi 38; Ar 69931mx

L53 ANSWER 43 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006312756 EMBASE

TITLE: Drug Insight: Clopidogrel nonresponsiveness.

AUTHOR: Gurbel P.A.; Tantry U.S.

CORPORATE SOURCE: P.A. Gurbel, Sinai Center for Thrombosis Research, 2401 West Belvedere Avenue, Baltimore, MD 21215, United States. pgurbel@lifebridgehealth.org

SOURCE: Nature Clinical Practice Cardiovascular Medicine, (2006) Vol. 3, No. 7, pp. 387-395. .

Refs: 60

ISSN: 1743-4297 E-ISSN: 1743-4300

PUBLISHER IDENT.: N0602

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 21 Jul 2006

Last Updated on STN: 21 Jul 2006

ABSTRACT: Platelet reactivity to agonists and subsequent activation are important factors that affect the development of atherothrombosis and resultant ischemic events. Pharmacologic intervention with clopidogrel and aspirin during acute **coronary** syndromes and **percutaneous ***coronary***** intervention is considered the gold standard for attenuating platelet activation and aggregation. Despite significant benefits reported with dual antiplatelet treatment in major clinical trials, the occurrence of adverse ischemic events, including stent thrombosis, remains a serious clinical problem. Nonresponsiveness, also called resistance, to current clopidogrel regimens might play a part in the occurrence of ischemic events. Various mechanisms have been implicated in nonresponsiveness to clopidogrel, including variability in intestinal absorption and hepatic conversion to the active metabolite, drug-drug interactions and receptor polymorphisms. Increased loading and maintenance doses and the use of new and more-potent P2Y(12)-receptor blockers might overcome the phenomenon of clopidogrel nonresponsiveness. The aim of this article is to provide a comprehensive and current review of clopidogrel response variability and nonresponsiveness. .COPYRG. 2006 Nature Publishing Group.

CONTROLLED TERM: Medical Descriptors:

*acute coronary syndrome: DR, drug resistance

*acute coronary syndrome: DT, drug therapy

*acute coronary syndrome: SU, surgery

*percutaneous coronary intervention

thrombocyte activation

thrombocyte aggregation inhibition

thrombosis: CO, complication

thrombosis: DT, drug therapy

thrombosis: PC, prevention

drug response

protein polymorphism

maintenance therapy

drug receptor binding

drug mechanism

laboratory test
drug metabolism
drug dose regimen
pharmacodynamics
bleeding: SI, side effect
cerebrovascular accident: CO, complication
cerebrovascular accident: DT, drug therapy
cerebrovascular accident: PC, prevention
heart infarction: CO, complication
heart infarction: DT, drug therapy
heart infarction: PC, prevention

drug bioavailability

drug absorption

human

clinical trial

review

priority journal

CONTROLLED TERM:

Drug Descriptors:

*clopidogrel: AE, adverse drug reaction

*clopidogrel: CT, clinical trial

*clopidogrel: CM, drug comparison

*clopidogrel: DO, drug dose

*clopidogrel: IT, drug interaction

*clopidogrel: DT, drug therapy

*clopidogrel: PK, pharmacokinetics

*clopidogrel: PD, pharmacology

*clopidogrel: PO, oral drug administration

cytochrome P450 3A4: EC, endogenous compound

rifampicin: IT, drug interaction

Hypericum perforatum extract: IT, drug interaction

erythromycin: IT, drug interaction

atorvastatin: IT, drug interaction

acetylsalicylic acid: AE, adverse drug reaction

acetylsalicylic acid: CT, clinical trial

acetylsalicylic acid: CB, drug combination

acetylsalicylic acid: CM, drug comparison

acetylsalicylic acid: DT, drug therapy

acetylsalicylic acid: PD, pharmacology

purine P2Y12 receptor: EC, endogenous compound

receptor blocking agent: CT, clinical trial

receptor blocking agent: CM, drug comparison

receptor blocking agent: DT, drug therapy

receptor blocking agent: PD, pharmacology

receptor blocking agent: PO, oral drug administration

azd 6140: CT, clinical trial

azd 6140: CM, drug comparison

azd 6140: DT, drug therapy

azd 6140: PD, pharmacology

azd 6140: PO, oral drug administration

cangrelor: CT, clinical trial

cangrelor: CM, drug comparison

cangrelor: DT, drug therapy

cangrelor: PD, pharmacology

cangrelor: PA, parenteral drug administration

prasugrel: AE, adverse drug reaction

prasugrel: CT, clinical trial

prasugrel: CB, drug combination

prasugrel: CM, drug comparison

prasugrel: DT, drug therapy

prasugrel: PD, pharmacology

prasugrel: PO, oral drug administration
unclassified drug
CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4,
94188-84-8; (cytochrome P450 3A4) 329736-03-0; (rifampicin)
13292-46-1; (erythromycin) 114-07-8, 70536-18-4;
(atorvastatin) 134523-00-5, 134523-03-8; (acetylsalicylic
acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6,
63781-77-1; (prasugrel) **389574-19-0**
CHEMICAL NAME: (1) Azd 6140; Aspirin
COMPANY NAME: (1) Astra Zeneca (Sweden); Medicines (United States); Lilly
(United States); Sankyo (United States)

L53 ANSWER 44 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights
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ACCESSION NUMBER: 2006229279 EMBASE
TITLE: Antiplatelet therapy: Current strategies and future trends.
AUTHOR: Tantry U.S.; Etherington A.; Bliden K.P.; Gurbel P.A.
CORPORATE SOURCE: Dr. P.A. Gurbel, Sinai Center for Thrombosis Research, 2401
W. Belvedere Ave., Baltimore, MD 21215, United States.
pgurbel@lifebridgehealth.org
SOURCE: Future Cardiology, (2006) Vol. 2, No. 3, pp. 343-366. .
Refs: 163
ISSN: 1479-6678 E-ISSN: 1744-8298
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Jun 2006
Last Updated on STN: 1 Jun 2006

ABSTRACT: Pharmacological management of thrombotic complications is strongly
influenced by antiplatelet treatment strategies. Recent clinical trials have
clearly indicated that current antiplatelet strategies may not inhibit
recurrent thrombotic events in selected patients and improvement is necessary.
Recently, there has been a gradual modification in the guidelines for
clopidogrel dosing. In addition, newly developed P2Y₁₂ receptor inhibitors
and thrombin inhibitors are undergoing Phase II and III clinical trials.
Moreover, research related to novel agents that interfere with other steps in
coagulation and platelet adhesion, and platelet thromboxane and thrombin
receptor blockers, show promise. An important future step will probably be the
development of personalized therapy based on defining the individual patient's
propensity for thrombosis through investigation of platelet-thrombin-fibrin
interactions. Such an approach will enhance the targeting of specific therapy
based on the pathophysiology of the individual patient. .COPYRG. 2006 Future
Medicine Ltd.

CONTROLLED TERM: Medical Descriptors:
*thrombosis: CO, complication
*thrombosis: DR, drug resistance
*thrombosis: DT, drug therapy
*thrombosis: PC, prevention
*anticoagulant therapy
*cardiovascular disease: DR, drug resistance
*cardiovascular disease: DT, drug therapy
*cardiovascular disease: PC, prevention
*cardiovascular disease: SU, surgery

recurrent disease: CO, complication
recurrent disease: DR, drug resistance
recurrent disease: DT, drug therapy
recurrent disease: PC, prevention
practice guideline
drug dose regimen
blood clotting
thrombocyte adhesion
individualization
treatment planning
drug targeting
pathophysiology
drug mechanism
primary prevention
secondary prevention
gastrointestinal hemorrhage: SI, side effect
bleeding: SI, side effect
 heart reinfarction: DR, drug resistance
 heart reinfarction: DT, drug therapy
 heart reinfarction: PC, prevention
systematic review
drug absorption
drug potentiation
human
nonhuman
clinical trial
meta analysis
review
priority journal

CONTROLLED TERM:

Drug Descriptors:
*antithrombocytic agent: AE, adverse drug reaction
*antithrombocytic agent: CT, clinical trial
*antithrombocytic agent: CB, drug combination
*antithrombocytic agent: CM, drug comparison
*antithrombocytic agent: DO, drug dose
*antithrombocytic agent: IT, drug interaction
*antithrombocytic agent: DT, drug therapy
*antithrombocytic agent: PK, pharmacokinetics
*antithrombocytic agent: PD, pharmacology
*antithrombocytic agent: PO, oral drug administration
*antithrombocytic agent: PA, parenteral drug administration
clopidogrel: AE, adverse drug reaction
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: CM, drug comparison
clopidogrel: DO, drug dose
clopidogrel: IT, drug interaction
clopidogrel: DT, drug therapy
clopidogrel: PK, pharmacokinetics
clopidogrel: PD, pharmacology
clopidogrel: PO, oral drug administration
purine P2Y₁₂ receptor: EC, endogenous compound
purinergic receptor blocking agent: CT, clinical trial
purinergic receptor blocking agent: CB, drug combination
purinergic receptor blocking agent: CM, drug comparison
purinergic receptor blocking agent: DT, drug therapy
purinergic receptor blocking agent: PK, pharmacokinetics
purinergic receptor blocking agent: PD, pharmacology
purinergic receptor blocking agent: PO, oral drug administration

purinergic receptor blocking agent: PA, parenteral drug administration
thrombin inhibitor: AE, adverse drug reaction
thrombin inhibitor: CT, clinical trial
thrombin inhibitor: CM, drug comparison
thrombin inhibitor: DT, drug therapy
thrombin inhibitor: PD, pharmacology
thromboxane: EC, endogenous compound
fibrin: EC, endogenous compound
thrombin: EC, endogenous compound
heparin: AE, adverse drug reaction
heparin: CT, clinical trial
heparin: CB, drug combination
heparin: CM, drug comparison
heparin: DT, drug therapy
heparin: PD, pharmacology
low molecular weight heparin: AE, adverse drug reaction
low molecular weight heparin: CT, clinical trial
low molecular weight heparin: CB, drug combination
low molecular weight heparin: CM, drug comparison
low molecular weight heparin: DT, drug therapy
low molecular weight heparin: PD, pharmacology
low molecular weight heparin: SC, subcutaneous drug administration
hirulog: AE, adverse drug reaction
hirulog: CT, clinical trial
hirulog: CM, drug comparison
hirulog: DT, drug therapy
hirulog: PD, pharmacology
acetylsalicylic acid: AE, adverse drug reaction
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: IT, drug interaction
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
anticoagulant agent: CT, clinical trial
anticoagulant agent: CM, drug comparison
anticoagulant agent: DT, drug therapy
anticoagulant agent: PK, pharmacokinetics
anticoagulant agent: PD, pharmacology
anticoagulant agent: PO, oral drug administration
azd 6140: CT, clinical trial
azd 6140: CM, drug comparison
azd 6140: DT, drug therapy
azd 6140: PK, pharmacokinetics
azd 6140: PD, pharmacology
azd 6140: PO, oral drug administration
cangrelor: CT, clinical trial
cangrelor: DT, drug therapy
cangrelor: PK, pharmacokinetics
cangrelor: PD, pharmacology
cangrelor: PA, parenteral drug administration
prasugrel: CT, clinical trial
prasugrel: CM, drug comparison
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
prasugrel: PO, oral drug administration
alteplase: DT, drug therapy
reteplase: DT, drug therapy

tenecteplase: DT, drug therapy
 warfarin: CB, drug combination
 warfarin: CM, drug comparison
 warfarin: DT, drug therapy
 ticlopidine: DT, drug therapy
 ticlopidine: PD, pharmacology
 fibrinogen receptor antagonist: AE, adverse drug reaction
 fibrinogen receptor antagonist: CT, clinical trial
 fibrinogen receptor antagonist: CB, drug combination
 fibrinogen receptor antagonist: CM, drug comparison
 fibrinogen receptor antagonist: DT, drug therapy
 fibrinogen receptor antagonist: PD, pharmacology
 abciximab: AE, adverse drug reaction
 abciximab: CT, clinical trial
 abciximab: CB, drug combination
 abciximab: CM, drug comparison
 abciximab: DT, drug therapy
 abciximab: PD, pharmacology
 eptifibatide: AE, adverse drug reaction
 eptifibatide: CT, clinical trial
 eptifibatide: CB, drug combination
 eptifibatide: CM, drug comparison
 eptifibatide: DT, drug therapy
 eptifibatide: PD, pharmacology
 tirofiban: CT, clinical trial
 tirofiban: CB, drug combination
 tirofiban: CM, drug comparison
 tirofiban: DT, drug therapy
 tirofiban: PD, pharmacology
 fibrinolytic agent: CT, clinical trial
 fibrinolytic agent: CB, drug combination
 fibrinolytic agent: DT, drug therapy
 metoprolol: CT, clinical trial
 metoprolol: CB, drug combination
 metoprolol: DT, drug therapy
 dipyridamole: CB, drug combination
 dipyridamole: CM, drug comparison
 dipyridamole: DT, drug therapy
 dipyridamole: PD, pharmacology
 cilostazol: DT, drug therapy
 cilostazol: PD, pharmacology
 unindexed drug
 unclassified drug
 arc 669931 mx

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4,
 94188-84-8; (thromboxane) 66719-58-2; (fibrin) 9001-31-4;
 (thrombin) 9002-04-4; (heparin) 37187-54-5, 8057-48-5,
 8065-01-8, 9005-48-5; (hirulog) 128270-60-0;
 (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4,
 53664-49-6, 63781-77-1; (prasugrel) 389574-19-0;
 (alteplase) 105857-23-6; (reteplase) 133652-38-7;
 (tenecteplase) 191588-94-0; (warfarin) 129-06-6, 2610-86-8,
 3324-63-8, 5543-58-8, 81-81-2; (ticlopidine) 53885-35-1,
 55142-85-3; (abciximab) 143653-53-6; (eptifibatide)
 148031-34-9; (tirofiban) 142373-60-2, 144494-65-5,
 150915-40-5; (metoprolol) 37350-58-6; (dipyridamole)
 58-32-2; (cilostazol) 73963-72-1

CHEMICAL NAME: (1) Azd 6140; (2) Cs 747; (3) Arc 669931 mx; Aspirin;
 Aggrastat; Reopro; Persantine

COMPANY NAME: (1) Astra Zeneca (United States); (2) Lilly (United

States); (3) Medicines (United States); Sanofi Synthelabo (France)

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ACCESSION NUMBER: 2006090617 EMBASE
TITLE: Regulation of platelet functions by P2 receptors.
AUTHOR: Gachet C.
CORPORATE SOURCE: C. Gachet, Institut National de la Sante et de la Recherche Medicale, Etablissement Francais du Sang-Alsace, Strasbourg 67065, France. christian.gachet@efs-alsace.fr
SOURCE: Annual Review of Pharmacology and Toxicology, (2006) Vol. 46, pp. 277-300. .
Refs: 149
ISSN: 0362-1642 CODEN: ARPTDI
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 025 Hematology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Mar 2006
Last Updated on STN: 16 Mar 2006

ABSTRACT: The main role of blood platelets is to ensure primary hemostasis, which is the maintenance of vessel integrity and cessation of bleeding upon injury. While playing a major part in acute arterial thrombosis, platelets are also involved in inflammation, atherosclerosis, and angiogenesis. ADP and ATP play a crucial role in platelet activation, and their receptors are potential targets for antithrombotic drugs. The ATP-gated cation channel P2X(1) and the two G protein-coupled ADP receptors, P2Y(1) and P2Y(12), selectively contribute to platelet aggregation and formation of a thrombus. Owing to its central role in the growth and stabilization of a thrombus, the P2Y(12) receptor is an established target of antithrombotic drugs such as clopidogrel. Studies in P2Y(1) and P2X(1) knockout mice and selective P2Y(1) and P2X(1) antagonists have shown that these receptors are also attractive targets for new antithrombotic compounds. The potential role of platelet P(2) receptors in the involvement of platelets in inflammatory processes is also discussed.
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CONTROLLED TERM: Medical Descriptors:
*thrombocyte function
*thrombocyte
hemostasis
bleeding
artery thrombosis
inflammation
atherosclerosis
angiogenesis
thrombocyte activation
thrombogenesis
drug targeting
human
nonhuman
clinical trial
review
priority journal
CONTROLLED TERM: Drug Descriptors:
*purine P2 receptor: EC, endogenous compound
adenosine diphosphate: PD, pharmacology

adenosine triphosphate: PD, pharmacology
anticoagulant agent: CT, clinical trial
anticoagulant agent: PD, pharmacology
purine P2X1 receptor: EC, endogenous compound
purine P2Y12 receptor: EC, endogenous compound
clopidogrel: PD, pharmacology
acetylsalicylic acid: PD, pharmacology
prostaglandin synthase inhibitor: PD, pharmacology
ticlopidine: PD, pharmacology
purinergic receptor blocking agent: PD, pharmacology
2' deoxy 6 n methyladenosine 3',5' bisphosphate: PD,
pharmacology
mrs 2500: PD, pharmacology
adrenalin: PD, pharmacology
serotonin: PD, pharmacology
suramin: PD, pharmacology
mrs 2279: PD, pharmacology
ar c 66096mx: PD, pharmacology
ar c 67085mx: PD, pharmacology
ar c 69931mx: PD, pharmacology
c 13307: PD, pharmacology
azd 6140: PD, pharmacology
prasugrel: PD, pharmacology
unclassified drug
nf 449

CAS REGISTRY NO.: (adenosine diphosphate) 20398-34-9, 58-64-0; (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (ticlopidine) 53885-35-1, 55142-85-3; (2' deoxy 6 n methyladenosine 3',5' bisphosphate) 101204-49-3; (adrenalin) 51-43-4, 55-31-2, 6912-68-1; (serotonin) 50-67-9; (suramin) 129-46-4, 145-63-1; (prasugrel) **389574-19-0**

CHEMICAL NAME: Mrs 2179; Mrs 2500; Nf 449; Mrs 2279; Ar c 66096mx; Ar c 69931mx; Ar c 67085mx; C 13307; Azd 6140; Cs 747; Ly 640315

L53 ANSWER 46 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006229269 EMBASE
TITLE: A point-of-care assay to measure platelet aggregation in patients taking clopidogrel.
AUTHOR: McLean D.S.; Cannon C.P.
CORPORATE SOURCE: Dr. D.S. McLean, 350 Longwood Ave., Boston, MA 02115, United States. dsmclean@partners.org
SOURCE: Future Cardiology, (2006) Vol. 2, No. 3, pp. 255-267. .
Refs: 75
ISSN: 1479-6678 E-ISSN: 1744-8298
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Jun 2006

Last Updated on STN: 1 Jun 2006

ABSTRACT: Clopidogrel is an important component of medical therapy for patients with acute coronary syndromes and those receiving coronary stents. Despite the use of clopidogrel, a significant number of patients experience recurrent adverse ischemic events. Inter-individual variability of platelet aggregation in response to clopidogrel may provide an explanation for some of these recurrent events, and small trials have linked clopidogrel resistance, as measured by platelet function tests, to adverse events. The VerifyNow® P2Y12 assay (Accumetrics, Inc., CA, USA) is a point-of-care device that can accurately and rapidly measure the degree of platelet inhibition in patients taking clopidogrel. This assay can identify patients with a poor response to clopidogrel, and could potentially lead to change in therapy. .COPYRG. 2006 Future Medicine Ltd.

CONTROLLED TERM: Medical Descriptors:
 *acute coronary syndrome: DR, drug resistance
 *acute coronary syndrome: DT, drug therapy
 *acute coronary syndrome: SU, surgery
 *acute coronary syndrome: TH, therapy
 *thrombocyte aggregation
 *bioassay
 drug use
 coronary stent
 heart muscle ischemia: DI, diagnosis
 heart muscle ischemia: ET, etiology
 heart muscle ischemia: SI, side effect
 individualization
 drug response
 thrombocyte function
 blood clotting parameters
 analytical equipment
 diagnostic accuracy
 drug mechanism
 enzyme inhibition
 gene activation
 drug safety
 heart infarction: DT, drug therapy
 percutaneous coronary intervention
 hematologic disease: SI, side effect
 drug dose regimen
 thrombosis: CO, complication
 bleeding: SI, side effect
 coronary artery bypass graft
 drug potentiation
 human
 clinical trial
 article
 priority journal

CONTROLLED TERM: Drug Descriptors:
 *clopidogrel: AE, adverse drug reaction
 *clopidogrel: CT, clinical trial
 *clopidogrel: CB, drug combination
 *clopidogrel: CM, drug comparison
 *clopidogrel: DO, drug dose
 *clopidogrel: DT, drug therapy
 *clopidogrel: PD, pharmacology
 ticlopidine: AE, adverse drug reaction
 ticlopidine: CB, drug combination
 ticlopidine: CM, drug comparison
 ticlopidine: DO, drug dose

ticlopidine: DT, drug therapy
 ticlopidine: PD, pharmacology
 prasugrel: PD, pharmacology
 adenosine diphosphate: EC, endogenous compound
 purine P2Y12 receptor: EC, endogenous compound
 purine P2Y1 receptor: EC, endogenous compound
 purine P2X receptor: EC, endogenous compound
 cyclic AMP: EC, endogenous compound
 G protein coupled receptor: EC, endogenous compound
 cytochrome P450 3A4: EC, endogenous compound
 antithrombocytic agent: AE, adverse drug reaction
 antithrombocytic agent: CT, clinical trial
 antithrombocytic agent: CB, drug combination
 antithrombocytic agent: CM, drug comparison
 antithrombocytic agent: DO, drug dose
 antithrombocytic agent: DT, drug therapy
 antithrombocytic agent: PD, pharmacology
 azd 6140: CT, clinical trial
 azd 6140: CM, drug comparison
 azd 6140: DT, drug therapy
 azd 6140: PD, pharmacology
 acetylsalicylic acid: AE, adverse drug reaction
 acetylsalicylic acid: CT, clinical trial
 acetylsalicylic acid: CM, drug comparison
 acetylsalicylic acid: DO, drug dose
 acetylsalicylic acid: DT, drug therapy
 creatine kinase: EC, endogenous compound
 prostaglandin E1: IT, drug interaction
 prostaglandin E1: PD, pharmacology
 cangrelor: IT, drug interaction
 cangrelor: PD, pharmacology
 fibrinogen receptor: EC, endogenous compound
 thrombin receptor activating peptide: EC, endogenous compound
 unclassified drug

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4,
 94188-84-8; (ticlopidine) 53885-35-1, 55142-85-3;
 (prasugrel) 389574-19-0; (adenosine diphosphate)
 20398-34-9, 58-64-0; (cyclic AMP) 60-92-4; (cytochrome P450
 3A4) 329736-03-0; (acetylsalicylic acid) 493-53-8, 50-78-2,
 53663-74-4, 53664-49-6, 63781-77-1; (creatine kinase)
 9001-15-4; (prostaglandin E1) 745-65-3; (thrombin receptor
 activating peptide) 137339-65-2
 CHEMICAL NAME: Cs 747; Azd 6140; Ar c69931 mx
 NAME OF PRODUCT: (1) VerifyNow P2Y12 assay
 COMPANY NAME: (1) Accumetrics (United States)

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ACCESSION NUMBER: 2006324391 EMBASE
 TITLE: Gateways to clinical trials.
 AUTHOR: Bayes M.; Rabasseda X.; Prous J.R.
 CORPORATE SOURCE: M. Bayes, Prous Science, S.A., P.O. Box 540, 08080
 Barcelona, Spain. mbayes@prous.com
 SOURCE: Methods and Findings in Experimental and Clinical
 Pharmacology, (2006) Vol. 28, No. 4, pp. 233-277. .
 Refs: 259
 ISSN: 0379-0355 CODEN: MFEPDX
 COUNTRY: Spain
 DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 21 Jul 2006
 Last Updated on STN: 21 Jul 2006

ABSTRACT: Gateways to Clinical Trials are a guide to the most recent clinical trials in current literature and congresses. The data in the following tables have been retrieved from the Clinical Trials Knowledge Area of Prous Science Integrity®, the drug discovery and development portal, <http://integrity.prous.com>. This issue focuses on the following selection of drugs: Adalimumab, adenosine triphosphate, alemtuzumab, alendronate sodium/cholecalciferol, aliskiren fumarate, AMG-0007, aminolevulinic acid methyl ester, anakinra, anidulafungin, aripiprazole, atomoxetine hydrochloride; Bevacizumab, bosentan; Calcipotriol/ β -methasone dipropionate, caldaret hydrate, caspofungin acetate, cetuximab, cinacalcet hydrochloride, clopidogrel, cocaine-BSA conjugate, conivaptan hydrochloride, Cypher; Darbepoetin alfa, delmitide, desloratadine, desmoteplase, desoxyepothilone B, disufenton sodium, DU-176b, duloxetine hydrochloride, dutasteride; EBV-specific CTLs, ecogranostim, edodekin alfa, efalizumab, eletriptan, emtricitabine, entecavir, erlotinib hydrochloride, ertapenem sodium, escitalopram oxalate, etoricoxib, everolimus, ezetimibe; Fanapanel; fondaparinux sodium; Gefitinib, GTI-2040, GW-501516; Her2 E75-peptide vaccine, human insulin; Ibogaine, icatibant acetate, Id-KLH vaccine, imatinib mesylate, immune globulin subcutaneous [human], indacaterol, inolimomab, ipilimumab, i.v. γ -globulin, ivabradine hydrochloride, ixabepilone; Lacosamide, lanthanum carbonate, lenalidomide, levocetirizine, levodopa methyl ester hydrochloride/carbidopa, levodopa/carbidopa/entacapone, lidocaine/prilocaine; Maraviroc, mecasermin, melevodopa hydrochloride, mepolizumab, mitumomab; Nesiritide; Omalizumab, oral insulin; Parathyroid hormone (human recombinant), patupilone, pegaptanib sodium, PEG-filgrastim, pemetrexed disodium, photochlor, pimecrolimus, posaconazole, prasterone, prasugrel, pregabalin, prilocaine, PRX-00023; QS-21; Ranibizumab, ranirestat, rhodamine 123, rotigaptide; Sarcosine, sirolimus-eluting stent, sitaxsentan sodium, solifenacin succinate, Staphylococcus aureus vaccine; Tadalafil, talactoferrin alfa, talaporfin sodium, Taxus, tecadenoson, tegaserod maleate, telithromycin, temsirolimus, tenofovir disoproxil fumarate, teriparatide, terutroban sodium, tesaglitazar, tesmilifene hydrochloride, TG-100115, tigecycline, torcetrapib; Ularitide; Valproic acid, sodium, voriconazole; Zotarolimus, zotarolimus-eluting stent. .COPYRG. 2006 Prous Science. All rights reserved.

CONTROLLED TERM: Medical Descriptors:
 *drug research
 anemia: DT, drug therapy
 eosinophilia: DR, drug resistance
 hypereosinophilic syndrome: DT, drug therapy
 neutropenia: DT, drug therapy
 hemophilia
 angina pectoris: DT, drug therapy
 drug eluting stent
 cardiovascular disease: DT, drug therapy
 cardiovascular disease: TH, therapy
 percutaneous transluminal angioplasty
 heart infarction: DT, drug therapy
 atherosclerosis: DT, drug therapy
 coronary artery disease: DT, drug therapy
 tachycardia: DT, drug therapy
 heart failure: DT, drug therapy
 congestive heart failure: DT, drug therapy
 hyponatremia: DT, drug therapy

erectile dysfunction: DT, drug therapy
hypertension: DT, drug therapy
granulomatosis: DT, drug therapy
Wegener granulomatosis: DT, drug therapy
vasculitis: DT, drug therapy
ischemia: DT, drug therapy
hypopituitarism: DT, drug therapy
eye allergy: DT, drug therapy
asthma: DT, drug therapy
conjunctivitis: DT, drug therapy
eczema: DT, drug therapy
rhinitis: DT, drug therapy
urticaria: DT, drug therapy
diabetes mellitus: DT, drug therapy
edema
retinopathy
retina macula degeneration
subretinal neovascularization
human
clinical trial
review

CONTROLLED TERM:

Drug Descriptors:
recombinant erythropoietin: CT, clinical trial
recombinant erythropoietin: DT, drug therapy
recombinant erythropoietin: SC, subcutaneous drug
administration
novel erythropoiesis stimulating protein: CT, clinical
trial
novel erythropoiesis stimulating protein: DT, drug therapy
novel erythropoiesis stimulating protein: SC, subcutaneous
drug administration
mepolizumab: CT, clinical trial
mepolizumab: DT, drug therapy
mepolizumab: IV, intravenous drug administration
caspofungin: CT, clinical trial
caspofungin: DT, drug therapy
etoricoxib: CT, clinical trial
etoricoxib: DT, drug therapy
etoricoxib: PO, oral drug administration
ivabradine: CT, clinical trial
ivabradine: DT, drug therapy
ivabradine: PO, oral drug administration
atenolol: CT, clinical trial
atenolol: DT, drug therapy
atenolol: PO, oral drug administration
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: DT, drug therapy
prasugrel: CT, clinical trial
prasugrel: CB, drug combination
prasugrel: DT, drug therapy
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: DT, drug therapy
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
heparin: CT, clinical trial
heparin: DT, drug therapy
heparin: IV, intravenous drug administration

rapamycin: CT, clinical trial
 rapamycin: DT, drug therapy
 cilostazol: CT, clinical trial
 cilostazol: CB, drug combination
 cilostazol: DT, drug therapy
 tecadenoson: CT, clinical trial
 tecadenoson: DT, drug therapy
 tecadenoson: IV, intravenous drug administration
 tg 100115: CT, clinical trial
 tg 100115: DT, drug therapy
 nesiritide: CT, clinical trial
 nesiritide: DT, drug therapy
 nesiritide: IV, intravenous drug administration
 diuretic agent: CT, clinical trial
 diuretic agent: CB, drug combination
 diuretic agent: DT, drug therapy
 diuretic agent: IV, intravenous drug administration
 glyceryl trinitrate: CT, clinical trial
 glyceryl trinitrate: CB, drug combination
 glyceryl trinitrate: DT, drug therapy
 glyceryl trinitrate: IV, intravenous drug administration
 placebo
 urodilatin: CT, clinical trial
 urodilatin: DT, drug therapy
 urodilatin: IV, intravenous drug administration
 conivaptan: CT, clinical trial
 conivaptan: DT, drug therapy
 conivaptan: IV, intravenous drug administration
 conivaptan: PO, oral drug administration
 tadalafil: CT, clinical trial
 tadalafil: DT, drug therapy
 immunoglobulin: CT, clinical trial
 immunoglobulin: DT, drug therapy
 immunoglobulin: IV, intravenous drug administration
 aliskiren: CT, clinical trial
 aliskiren: DT, drug therapy
 prasterone: CT, clinical trial
 prasterone: DT, drug therapy
 levocetirizine: CT, clinical trial
 levocetirizine: DT, drug therapy
 levocetirizine: PO, oral drug administration
 pegaptanib: CT, clinical trial
 ranibizumab: CT, clinical trial
 unindexed drug
 unclassified drug

CAS REGISTRY NO.: (recombinant erythropoietin) 113427-24-0, 122312-54-3,
 130455-76-4; (mepolizumab) 196078-29-2; (caspofungin)
 189768-38-5; (etoricoxib) 202409-33-4, 202409-40-3;
 (ivabradine) 148849-67-6, 148870-80-8, 155974-00-8;
 (atenolol) 29122-68-7; (acetylsalicylic acid) 493-53-8,
 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (prasugrel)
 389574-19-0; (clopidogrel) 113665-84-2,
 120202-66-6, 90055-48-4, 94188-84-8; (paclitaxel)
 33069-62-4; (heparin) 37187-54-5, 8057-48-5, 8065-01-8,
 9005-48-5; (rapamycin) 53123-88-9; (cilostazol) 73963-72-1;
 (tecadenoson) 204512-90-3; (nesiritide) 124584-08-3,
 189032-40-4; (glyceryl trinitrate) 55-63-0; (urodilatin)
 115966-23-9; (conivaptan) 168626-94-6, 210101-16-9;
 (tadalafil) 171596-29-5; (immunoglobulin) 9007-83-4;
 (aliskiren) 173334-57-1, 173334-58-2, 173399-03-6;

(prasterone) 53-43-0; (levocetirizine) 130018-77-8;
(pegaptanib) 222716-86-1; (ranibizumab) 347396-82-1
CHEMICAL NAME: Aspirin; Tg 100115

L53 ANSWER 48 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006229289 EMBASE
TITLE: Clopidogrel resistance: Fact and fiction.
AUTHOR: van Werkum J.W.; Heestermans A.A.C.M.; Deneer V.H.M.; Hackeng C.M.; ten Berg J.M.
CORPORATE SOURCE: J.M. ten Berg, Department of Cardiology, St. Antonius Hospital, PO Box 2500, 3435 CM Nieuwegein, Netherlands. berg03@antonius.net
SOURCE: Future Cardiology, (2006) Vol. 2, No. 2, pp. 215-228. . Refs: 113
ISSN: 1479-6678 E-ISSN: 1744-8298
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Jun 2006
Last Updated on STN: 1 Jun 2006

ABSTRACT: The antiplatelet agent clopidogrel in combination with aspirin has been shown to reduce thrombotic events in patients with acute coronary syndromes and/or who are undergoing **percutaneous coronary** intervention. However, a large interindividual response variability to clopidogrel has been described. The reported rates of inadequate clopidogrel response vary considerably depending on the definition and methodologies used to measure the inhibition of platelet function. Recently, several (small) studies have demonstrated the clinical relevance of an inadequate response to clopidogrel. Moreover, several factors have been associated with a high interindividual variability in response to clopidogrel. These are: dosing, impaired intestinal absorption, cytochrome P450 3A4 and 3A5 activity, drug-drug interactions, polymorphisms of the receptors involved in the process of arterial thrombosis and hemostasis, and the method of measurement of platelet function. Future research for the evaluation of clopidogrel resistance should be based on the assessment of selective P2Y₁₂ receptor inhibition (e.g., the vasodilator-stimulated phosphoprotein-assay or the measurement of stabilization of platelet aggregates) with quick and simple tests. Only then can we reveal the true prevalence and impact of clopidogrel resistance. .COPYRG. 2006 Future Medicine Ltd.

CONTROLLED TERM: Medical Descriptors:
*drug resistance
thrombosis: DT, drug therapy
thrombosis: PC, prevention
acute coronary syndrome: SU, surgery
percutaneous coronary intervention
drug response
methodology
thrombocyte function
intestine absorption
enzyme activity
genetic polymorphism
artery thrombosis

hemostasis
drug research
protein determination
thrombocyte aggregation
thrombogenesis
drug mechanism
drug dose regimen
drug blood level
drug metabolism
drug antagonism
human
clinical trial
review
priority journal

CONTROLLED TERM:

Drug Descriptors:

*clopidogrel: CT, clinical trial
*clopidogrel: CB, drug combination
*clopidogrel: CR, drug concentration
*clopidogrel: DO, drug dose
*clopidogrel: IT, drug interaction
*clopidogrel: DT, drug therapy
*clopidogrel: PK, pharmacokinetics
*clopidogrel: PD, pharmacology
*clopidogrel: PO, oral drug administration
antithrombocytic agent: CT, clinical trial
antithrombocytic agent: CB, drug combination
antithrombocytic agent: CR, drug concentration
antithrombocytic agent: DO, drug dose
antithrombocytic agent: IT, drug interaction
antithrombocytic agent: DT, drug therapy
antithrombocytic agent: PK, pharmacokinetics
antithrombocytic agent: PD, pharmacology
antithrombocytic agent: PO, oral drug administration
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: DT, drug therapy
cytochrome P450 3A4: EC, endogenous compound
cytochrome P450 3A5: EC, endogenous compound
purine P2Y12 receptor: EC, endogenous compound
vasodilator stimulated phosphoprotein: EC, endogenous compound
adenosine diphosphate
fibrinogen receptor: EC, endogenous compound
thrombin: EC, endogenous compound
fibrin: EC, endogenous compound
atorvastatin: CB, drug combination
atorvastatin: IT, drug interaction
simvastatin: CB, drug combination
simvastatin: IT, drug interaction
prasugrel: DV, drug development
cangrelor: DV, drug development
purinergic receptor blocking agent: DV, drug development
azd 6140: DV, drug development
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: DT, drug therapy
unclassified drug
(clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4,
94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2,
53663-74-4, 53664-49-6, 63781-77-1; (cytochrome P450 3A4)
329736-03-0; (cytochrome P450 3A5) 336874-97-6; (adenosine
diphosphate) 20398-34-9, 58-64-0; (thrombin) 9002-04-4;

CAS REGISTRY NO.:

(fibrin) 9001-31-4; (atorvastatin) 134523-00-5,
134523-03-8; (simvastatin) 79902-63-9; (prasugrel)
389574-19-0

CHEMICAL NAME: Aspirin; Azd 6140

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ACCESSION NUMBER: 2006155767 EMBASE

TITLE: Can clopidogrel and aspirin lower mortality in patients with acute myocardial infarction?.

AUTHOR: Bhatt D.L.

CORPORATE SOURCE: Prof. D.L. Bhatt, Cleveland Clinic, Department of Cardiovascular Medicine, 9500 Euclid Avenue, Cleveland, OH 44195, United States. bhatttd@ccf.org

SOURCE: Nature Clinical Practice Cardiovascular Medicine, (2006) Vol. 3, No. 4, pp. 182-183. .
Refs: 5

ISSN: 1743-4297 E-ISSN: 1743-4300

PUBLISHER IDENT.: N0508

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

ENTRY DATE: Entered STN: 12 Apr 2006

Last Updated on STN: 12 Apr 2006

CONTROLLED TERM: Medical Descriptors:

*mortality

*anticoagulant therapy

*acute heart infarction: DT, drug therapy

ST segment elevation

questionnaire

patient compliance

cause of death

outcomes research

heart reinfarction: CO, complication

heart reinfarction: DT, drug therapy

heart reinfarction: PC, prevention

stroke: CO, complication

stroke: DT, drug therapy

stroke: PC, prevention

bleeding: SI, side effect

drug safety

drug efficacy

acute coronary syndrome: DT, drug therapy

angiocardiology

thrombocyte aggregation inhibition

brain hemorrhage: SI, side effect

drug targeting

human

clinical trial

short survey

priority journal

CONTROLLED TERM: Drug Descriptors:

*clopidogrel: AE, adverse drug reaction

*clopidogrel: CT, clinical trial

*clopidogrel: CB, drug combination

*clopidogrel: DT, drug therapy
*acetylsalicylic acid: AE, adverse drug reaction
*acetylsalicylic acid: CT, clinical trial
*acetylsalicylic acid: CB, drug combination
*acetylsalicylic acid: DT, drug therapy
placebo
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: CB, drug combination
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: IV, intravenous drug administration
heparin: DT, drug therapy
low molecular weight heparin: DT, drug therapy
fibrinolytic agent: CB, drug combination
fibrinolytic agent: DT, drug therapy
prasugrel: AE, adverse drug reaction
prasugrel: CT, clinical trial
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
adenosine diphosphate: EC, endogenous compound
receptor blocking agent: AE, adverse drug reaction
receptor blocking agent: CT, clinical trial
receptor blocking agent: DT, drug therapy
receptor blocking agent: PD, pharmacology
azd 6140: AE, adverse drug reaction
azd 6140: CT, clinical trial
azd 6140: DT, drug therapy
azd 6140: PD, pharmacology
cangrelor: AE, adverse drug reaction
cangrelor: CT, clinical trial
cangrelor: DT, drug therapy
cangrelor: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (prasugrel) 389574-19-0; (adenosine diphosphate) 20398-34-9, 58-64-0
CHEMICAL NAME: Aspirin; Azd 6140

L53 ANSWER 50 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006017817 EMBASE
TITLE: Platelets in atherothrombosis.
AUTHOR: Vorchheimer D.A.; Becker R.
CORPORATE SOURCE: Dr. D.A. Vorchheimer, Zena and Michael Wiener Cardiovascular Institute, Mount Sinai School of Medicine, Box 1030, 1 Gustave Levy Pl, New York, NY 10029, United States. david.vorchheimer@msnyuhealth.org
SOURCE: Mayo Clinic Proceedings, (2006) Vol. 81, No. 1, pp. 59-68.
Refs: 89
ISSN: 0025-6196 CODEN: MACPAJ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Feb 2006
Last Updated on STN: 2 Feb 2006

ABSTRACT: Atherosclerosis is a diffuse, systemic disease that affects the coronary, cerebral, and peripheral arterial trees. Disruption of atherosclerotic plaques leads to thrombus formation and arterial occlusion. This unpredictable and potentially life-threatening atherothrombotic sequence underlies clinical events such as angina, myocardial infarction, transient ischemic attacks, and stroke. One of the key components of a clot is the platelet. Although it was previously thought that platelets were relatively inactive cells that merely provided a framework for the attachment of other cells and proteins to mechanically stop bleeding due to injury, it is now known that this is not the case. Platelets secrete and express a large number of substances that are crucial mediators of both coagulation and inflammation. This article reviews the centrality of the platelet in atherothrombosis and briefly looks at the efficacy of antiplatelet agents in preventing and treating cardiovascular disease. .COPYRGT. 2006 Mayo Foundation for Medical Education and Research.

CONTROLLED TERM: Medical Descriptors:

- *thrombocyte
 - *thrombosis: ET, etiology
 - *atherosclerosis: ET, etiology
- *atherothrombosis: ET, etiology
- atherosclerotic plaque
- thrombogenesis
- artery occlusion
- disease course
- angina pectoris
- heart infarction
- transient ischemic attack
- stroke: SI, side effect
- blood clotting
- cell adhesion
- cell secretion
- inflammation
 - cardiovascular disease: DT, drug therapy
 - cardiovascular disease: ET, etiology
 - cardiovascular disease: PC, prevention
- drug efficacy
- gastrointestinal symptom: SI, side effect
- intestine ulcer: SI, side effect
- bleeding: SI, side effect
- human
- clinical trial
- review

Drug Descriptors:

- antithrombocytic agent: AE, adverse drug reaction
- antithrombocytic agent: CT, clinical trial
- antithrombocytic agent: DT, drug therapy
- antithrombocytic agent: PD, pharmacology
 - acetylsalicylic acid: AE, adverse drug reaction
 - acetylsalicylic acid: CT, clinical trial
 - acetylsalicylic acid: CB, drug combination
 - acetylsalicylic acid: CM, drug comparison
 - acetylsalicylic acid: DO, drug dose
 - acetylsalicylic acid: DT, drug therapy
 - acetylsalicylic acid: PD, pharmacology

thieno[3,2 c]pyridine derivative: AE, adverse drug reaction
thieno[3,2 c]pyridine derivative: CT, clinical trial
thieno[3,2 c]pyridine derivative: CB, drug combination
thieno[3,2 c]pyridine derivative: DT, drug therapy
thieno[3,2 c]pyridine derivative: PD, pharmacology
clopidogrel: AE, adverse drug reaction
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: CM, drug comparison
clopidogrel: DO, drug dose
clopidogrel: DT, drug therapy
clopidogrel: PD, pharmacology
ticlopidine: DT, drug therapy
ticlopidine: PD, pharmacology
prasugrel: CT, clinical trial
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
metoprolol: CT, clinical trial
metoprolol: CB, drug combination
metoprolol: DT, drug therapy
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: AD, drug administration
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: PD, pharmacology
fibrinogen receptor antagonist: IV, intravenous drug
administration
fibrinogen receptor antagonist: PO, oral drug
administration
abciximab: DT, drug therapy
abciximab: PD, pharmacology
eptifibatide: DT, drug therapy
eptifibatide: PK, pharmacokinetics
eptifibatide: PD, pharmacology
tirofiban: DT, drug therapy
tirofiban: PK, pharmacokinetics
tirofiban: PD, pharmacology

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4,
53664-49-6, 63781-77-1; (clopidogrel) 113665-84-2,
120202-66-6, 90055-48-4, 94188-84-8; (ticlopidine)
53885-35-1, 55142-85-3; (prasugrel) 389574-19-0;
(metoprolol) 37350-58-6; (abciximab) 143653-53-6;
(eptifibatide) 148031-34-9; (tirofiban) 142373-60-2,
144494-65-5, 150915-40-5

CHEMICAL NAME: Aspirin

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ACCESSION NUMBER: 2006118487 EMBASE

TITLE: [Molecular target and clinical use of antithrombotic drugs].

FARMACI ANTI-TROMBOTICI. BERSAGLI MOLECOLARI E USO CLINICO.

AUTHOR: Evangelista V.; Totani L.

CORPORATE SOURCE: V. Evangelista, Laboratorio di Biologia e Farmacologia Vascolare, Dipartimento di Epidemiologia Clinica e Farmacologia, Consorzio Mario Negri Sud, S. Maria Imbaro CH
SOURCE: Giornale Italiano di Farmacia Clinica, (2005) Vol. 19, No. 4, pp. 399-407. .

Refs: 14

ISSN: 1120-3749 CODEN: GIFCEN

COUNTRY: Italy

DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index

LANGUAGE: Italian

SUMMARY LANGUAGE: English; Italian

ENTRY DATE: Entered STN: 31 Mar 2006

Last Updated on STN: 31 Mar 2006

ABSTRACT: Thrombosis plays a central role in the atherosclerotic process, determining progression and acute ischemic complications. The results of large scale clinical trials demonstrated the efficacy of anti-thrombotic therapies in the acute and chronic treatment of the cardiovascular disease. Anti-platelet and anti-coagulant drugs, alone or together with revascularization procedures such as thrombolysis, **percutaneous coronary** interventions or **coronary** artery by-pass, represent the mainstays of treatment of athero-thrombosis. Available drugs: aspirin, ticlopidine, clopidogrel, dipyridamole and GPIIb/IIIa inhibitors, concerning the platelet side; heparin, low molecular weight heparin, direct and indirect inhibitors of factor Xa, thrombin inhibitors and oral anticoagulants, for the coagulation side, target specific molecular mechanisms within the pathways of platelet activation and of the coagulation cascade. Moreover new drugs against new targets are currently tested in preclinical and clinical studies. This brief review summarizes the basic pharmacological mechanisms of the most important anti-thrombotic drugs and, on the basis of recent guidelines, their clinical use.

CONTROLLED TERM: Medical Descriptors:
*drug targeting
thrombosis
atherosclerosis
ischemia: CO, complication
disease course
cardiovascular disease: DT, drug therapy
revascularization
blood clot lysis
percutaneous coronary intervention
coronary artery bypass graft
practice guideline
stroke: DT, drug therapy
human
short survey

CONTROLLED TERM: Drug Descriptors:
*anticoagulant agent: DT, drug therapy
*anticoagulant agent: PD, pharmacology
*anticoagulant agent: PO, oral drug administration
antithrombotic agent: DT, drug therapy
antithrombotic agent: PD, pharmacology
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
ticlopidine: DT, drug therapy
ticlopidine: PD, pharmacology
clopidogrel: DT, drug therapy
clopidogrel: PD, pharmacology
dipyridamole: DT, drug therapy
dipyridamole: PD, pharmacology
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: PD, pharmacology
heparin: DT, drug therapy
heparin: PD, pharmacology
low molecular weight heparin: DT, drug therapy

low molecular weight heparin: PD, pharmacology
 blood clotting factor 10a inhibitor: DT, drug therapy
 blood clotting factor 10a inhibitor: PD, pharmacology
 thrombin inhibitor: DT, drug therapy
 thrombin inhibitor: PD, pharmacology
 prasugrel: DT, drug therapy
 prasugrel: PD, pharmacology
 arc 69931rx: DT, drug therapy
 arc 69931rx: PD, pharmacology
 arc 69931mx: DT, drug therapy
 arc 69931mx: PD, pharmacology
 abciximab: DT, drug therapy
 abciximab: PD, pharmacology
 eptifibatide: DT, drug therapy
 eptifibatide: PD, pharmacology
 tirofiban: DT, drug therapy
 tirofiban: PD, pharmacology
 2 [4 [(1 acetimidoyl 3 pyrrolidinyl)oxy]phenyl] 3 (7
 amidino 2 naphthyl)propionic acid: DT, drug therapy
 2 [4 [(1 acetimidoyl 3 pyrrolidinyl)oxy]phenyl] 3 (7
 amidino 2 naphthyl)propionic acid: PD, pharmacology
 fondaparinux: DT, drug therapy
 fondaparinux: PD, pharmacology
 idraparinux: DT, drug therapy
 idraparinux: PD, pharmacology
 antivitamin K: DT, drug therapy
 antivitamin K: PD, pharmacology
 warfarin: DT, drug therapy
 warfarin: PD, pharmacology
 blood clotting factor 7a inhibitor: DT, drug therapy
 blood clotting factor 7a inhibitor: PD, pharmacology
 hirudin: DT, drug therapy
 hirudin: PD, pharmacology
 hirulog: DT, drug therapy
 hirulog: PD, pharmacology
 argatroban: DT, drug therapy
 argatroban: PD, pharmacology
 ximelagatran: DT, drug therapy
 ximelagatran: PD, pharmacology
 lamifiban: DT, drug therapy
 lamifiban: PD, pharmacology
 rapamycin
 unindexed drug
 unclassified drug
 CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4,
 53664-49-6, 63781-77-1; (ticlopidine) 53885-35-1,
 55142-85-3; (clopidogrel) 113665-84-2, 120202-66-6,
 90055-48-4, 94188-84-8; (dipyridamole) 58-32-2; (heparin)
 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (prasugrel)
 389574-19-0; (abciximab) 143653-53-6;
 (eptifibatide) 148031-34-9; (tirofiban) 142373-60-2,
 144494-65-5, 150915-40-5; (2 [4 [(1 acetimidoyl 3
 pyrrolidinyl)oxy]phenyl] 3 (7 amidino 2 naphthyl)propionic
 acid) 155204-81-2; (fondaparinux) 104993-28-4, 114870-03-0;
 (idraparinux) 149920-56-9, 162610-17-5; (warfarin)
 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2;
 (hirudin) 8001-27-2; (hirulog) 128270-60-0; (argatroban)
 74863-84-6; (ximelagatran) 192939-46-1, 260790-58-7;
 (lamifiban) 144412-49-7; (rapamycin) 53123-88-9
 CHEMICAL NAME: Arc 69931rx; Arc 69931mx; Dx 9065

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ACCESSION NUMBER: 2006043777 EMBASE

TITLE: Best of TCT 2005.

AUTHOR: Faxon D.P.; Jacobs A.K.; Lepor N.E.; Yeung A.C.

CORPORATE SOURCE: Dr. D.P. Faxon, The University of Chicago Pritzker School of Medicine, Chicago, IL, United States

SOURCE: Reviews in Cardiovascular Medicine, (2005) Vol. 6, No. 4, pp. 214-221. .
ISSN: 1530-6550 CODEN: RCMEC5

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

ENTRY DATE: Entered STN: 3 Mar 2006
Last Updated on STN: 3 Mar 2006

CONTROLLED TERM: Medical Descriptors:
 *cardiovascular disease: DI, diagnosis
 *cardiovascular disease: DT, drug therapy
 *cardiovascular disease: PC, prevention
 *cardiovascular disease: SU, surgery
 *cardiovascular disease: TH, therapy
 drug eluting stent
 drug delivery system
 coronary stent
 angiocardiology
 percutaneous coronary intervention
 heart infarction: DI, diagnosis
 heart infarction: DT, drug therapy
 heart infarction: PC, prevention
 heart infarction: SU, surgery
 heart infarction: TH, therapy
 in-stent restenosis: CO, complication
 in-stent restenosis: DT, drug therapy
 in-stent restenosis: RT, radiotherapy
 thrombosis: CO, complication
 thrombosis: DT, drug therapy
 thrombosis: PC, prevention
 angioplasty
 coronary artery disease: DI, diagnosis
 coronary artery disease: DT, drug therapy
 coronary artery disease: PC, prevention
 coronary artery disease: SU, surgery
 coronary artery disease: TH, therapy
 dose response
 thrombocyte activation
 drug megadose
 thrombocyte aggregation inhibition
 drug absorption
 low drug dose
 treatment outcome
 stable angina pectoris
 ST segment elevation
 heart atrium fibrillation
 drug contraindication
 incidence

cerebrovascular accident
risk assessment
bleeding: SI, side effect
statistical significance
brachytherapy
intermethod comparison
clinical practice
coronary artery bypass surgery
disease severity
atherectomy
heart left ventricle ejection fraction
survival
drug efficacy
follow up
human
clinical trial
review
Drug Descriptors:
polymer
rapamycin
paclitaxel
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: DO, drug dose
clopidogrel: PK, pharmacokinetics
clopidogrel: PD, pharmacology
clopidogrel: PO, oral drug administration
prasugrel: DT, drug therapy
prasugrel: PD, pharmacology
heparin: AE, adverse drug reaction
heparin: CT, clinical trial
heparin: CB, drug combination
heparin: DT, drug therapy
heparin: PD, pharmacology
abciximab: CT, clinical trial
abciximab: CB, drug combination
abciximab: CM, drug comparison
abciximab: DT, drug therapy
hirulog: AE, adverse drug reaction
hirulog: CT, clinical trial
hirulog: CB, drug combination
hirulog: DT, drug therapy
warfarin: CT, clinical trial
warfarin: DT, drug therapy
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: CB, drug combination
fibrinogen receptor antagonist: CM, drug comparison
fibrinogen receptor antagonist: DT, drug therapy
tirofiban: CT, clinical trial
tirofiban: CB, drug combination
tirofiban: CM, drug comparison
tirofiban: DO, drug dose
tirofiban: DT, drug therapy
nitinol
politef

CAS REGISTRY NO.: (rapamycin) 53123-88-9; (paclitaxel) 33069-62-4;
(clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4,
94188-84-8; (prasugrel) 389574-19-0; (heparin)
37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (abciximab)
143653-53-6; (hirulog) 128270-60-0; (warfarin) 129-06-6,

2610-86-8, 3324-63-8, 5543-58-8, 81-81-2; (tirofiban)
142373-60-2, 144494-65-5, 150915-40-5; (nitinol)
52013-44-2; (politef) 9002-84-0, 9039-02-5

L53 ANSWER 53 OF 56 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006043780 EMBASE
TITLE: Use of antiplatelet agents and anticoagulants for cardiovascular disease: Current standards and best practices.
AUTHOR: Faxon D.P.
CORPORATE SOURCE: Dr. D.P. Faxon, Section of Cardiology, University of Chicago, Chicago, IL, United States
SOURCE: Reviews in Cardiovascular Medicine, (2005) Vol. 6, No. SUPPL. 4, pp. S3-S14. .
Refs: 42
ISSN: 1530-6550 CODEN: RCMEC5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2006
Last Updated on STN: 3 Mar 2006

ABSTRACT: Thrombosis superimposed on arteriosclerosis is the principal cause of mortality and morbidity in patients with arteriosclerosis. The use of antiplatelet agents and anticoagulants in the treatment of arteriosclerosis is well established, based on many large randomized trials. Aspirin is indicated for primary prevention in patients at increased risk of developing symptomatic atherosclerotic vascular disease. For patients with known vascular disease, antiplatelet therapy with aspirin is a well-established treatment. For high-risk patients such as those with acute coronary syndromes (ACS; unstable angina, myocardial infarction), dual antiplatelet therapy with aspirin and clopidogrel is indicated, based on results of the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial. Platelet glycoprotein IIb/IIIa agents are powerful inhibitors of platelet function and are also effective in ACS, but the benefit is confined to high-risk patients. Anticoagulation with heparin or low-molecular-weight heparin (eg, enoxaparin) is also effective, with an approximately 50% reduction in cardiovascular events. These agents are also indicated for patients undergoing ***percutaneous*** coronary intervention. Prolonged dual antiplatelet therapy (at least 6 months) is recommended for patients receiving drug-eluting stents. The efficacy of antiplatelet therapy is thus well established in treating atherothrombosis, but aggressive therapy is associated with an increased bleeding risk. Newer agents may provide improved efficacy with a lower risk of bleeding. .COPYRGHT. 2005 MedReviews, LLC.

CONTROLLED TERM: Medical Descriptors:
*cardiovascular disease: DT, drug therapy
*cardiovascular disease: PC, prevention
practice guideline
good clinical practice
thrombosis: CO, complication
thrombosis: DR, drug resistance
thrombosis: DT, drug therapy
thrombosis: PC, prevention

arteriosclerosis: DT, drug therapy
 coronary artery disease: DT, drug therapy
 acute coronary syndrome: DT, drug therapy
 acute heart infarction: DT, drug therapy
 unstable angina pectoris: DT, drug therapy
 unstable angina pectoris: PC, prevention
 mortality
 morbidity
 treatment indication
 primary prevention
 atherosclerosis: DT, drug therapy
 atherosclerosis: PC, prevention
 high risk patient
 risk assessment
 thrombocyte function
 anticoagulation
 risk reduction
 percutaneous coronary intervention
 drug eluting stent
 drug efficacy
 disease association
 bleeding: PC, prevention
 bleeding: SI, side effect
 cerebrovascular accident: CO, complication
 cerebrovascular accident: DT, drug therapy
 cerebrovascular accident: PC, prevention
 renovascular disease: CO, complication
 renovascular disease: DT, drug therapy
 renovascular disease: PC, prevention
 peripheral vascular disease: CO, complication
 peripheral vascular disease: DT, drug therapy
 peripheral vascular disease: PC, prevention
 disease course
 pathophysiology
 thrombogenicity
 systematic review
 thrombocyte aggregation inhibition
 antiinflammatory activity
 gastrointestinal hemorrhage: SI, side effect
 drug megadose
 drug safety
 drug absorption
 drug potency
 drug half life
 secondary prevention
 low drug dose
 human
 clinical trial
 meta analysis
 article

CONTROLLED TERM:

Drug Descriptors:
 *antithrombocytic agent: AE, adverse drug reaction
 *antithrombocytic agent: CT, clinical trial
 *antithrombocytic agent: CB, drug combination
 *antithrombocytic agent: DT, drug therapy
 *antithrombocytic agent: PD, pharmacology
 *anticoagulant agent: AE, adverse drug reaction
 *anticoagulant agent: CT, clinical trial
 *anticoagulant agent: CB, drug combination
 *anticoagulant agent: CM, drug comparison

*anticoagulant agent: DT, drug therapy
*anticoagulant agent: PK, pharmacokinetics
acetylsalicylic acid: AE, adverse drug reaction
acetylsalicylic acid: CT, clinical trial
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: DO, drug dose
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
clopidogrel: AE, adverse drug reaction
clopidogrel: CT, clinical trial
clopidogrel: CB, drug combination
clopidogrel: CM, drug comparison
clopidogrel: DO, drug dose
clopidogrel: DT, drug therapy
clopidogrel: PK, pharmacokinetics
clopidogrel: PD, pharmacology
ticlopidine: AE, adverse drug reaction
ticlopidine: CB, drug combination
ticlopidine: CM, drug comparison
ticlopidine: DO, drug dose
ticlopidine: DT, drug therapy
ticlopidine: PK, pharmacokinetics
ticlopidine: PD, pharmacology
prasugrel: CT, clinical trial
prasugrel: CM, drug comparison
prasugrel: DT, drug therapy
prasugrel: PK, pharmacokinetics
prasugrel: PD, pharmacology
fibrinogen receptor antagonist: CT, clinical trial
fibrinogen receptor antagonist: CB, drug combination
fibrinogen receptor antagonist: CM, drug comparison
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: PK, pharmacokinetics
fibrinogen receptor antagonist: PD, pharmacology
abciximab: CM, drug comparison
abciximab: DT, drug therapy
abciximab: PK, pharmacokinetics
abciximab: PD, pharmacology
eptifibatide: CT, clinical trial
eptifibatide: CB, drug combination
eptifibatide: CM, drug comparison
eptifibatide: DT, drug therapy
eptifibatide: PD, pharmacology
tirofiban: CT, clinical trial
tirofiban: CB, drug combination
tirofiban: CM, drug comparison
tirofiban: DT, drug therapy
tirofiban: PD, pharmacology
heparin: AE, adverse drug reaction
heparin: CT, clinical trial
heparin: CB, drug combination
heparin: CM, drug comparison
heparin: DT, drug therapy
heparin: PD, pharmacology
low molecular weight heparin: AE, adverse drug reaction
low molecular weight heparin: CT, clinical trial
low molecular weight heparin: CB, drug combination
low molecular weight heparin: CM, drug comparison
low molecular weight heparin: DT, drug therapy

low molecular weight heparin: PK, pharmacokinetics
 enoxaparin: AE, adverse drug reaction
 enoxaparin: CT, clinical trial
 enoxaparin: CM, drug comparison
 enoxaparin: DT, drug therapy
 enoxaparin: SC, subcutaneous drug administration
 dalteparin: DT, drug therapy
 blood clotting factor 10a inhibitor: CT, clinical trial
 blood clotting factor 10a inhibitor: CM, drug comparison
 blood clotting factor 10a inhibitor: DT, drug therapy
 blood clotting factor 10a inhibitor: PK, pharmacokinetics
 blood clotting factor 10a inhibitor: PD, pharmacology
 fondaparinux: CT, clinical trial
 fondaparinux: CM, drug comparison
 fondaparinux: DT, drug therapy
 fondaparinux: PK, pharmacokinetics
 fondaparinux: PD, pharmacology
 warfarin: AE, adverse drug reaction
 warfarin: CT, clinical trial
 warfarin: CB, drug combination
 warfarin: CM, drug comparison
 warfarin: DT, drug therapy
 warfarin: PK, pharmacokinetics
 warfarin: PO, oral drug administration
 thrombin inhibitor: CM, drug comparison
 thrombin inhibitor: DT, drug therapy
 thrombin inhibitor: PD, pharmacology
 hirulog: DT, drug therapy
 hirulog: IV, intravenous drug administration
 argatroban: DT, drug therapy
 argatroban: IV, intravenous drug administration
 ximelagatran: DT, drug therapy
 ximelagatran: PO, oral drug administration
 placebo
 fibrinolytic agent: DT, drug therapy
 streptokinase: DT, drug therapy
 reteplase: CT, clinical trial
 reteplase: CB, drug combination
 reteplase: DT, drug therapy
 tenecteplase: DT, drug therapy
 alteplase: DT, drug therapy

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4,
 53664-49-6, 63781-77-1; (clopidogrel) 113665-84-2,
 120202-66-6, 90055-48-4, 94188-84-8; (ticlopidine)
 53885-35-1, 55142-85-3; (prasugrel) **389574-19-0**;
 (abciximab) 143653-53-6; (eptifibatide) 148031-34-9;
 (tirofiban) 142373-60-2, 144494-65-5, 150915-40-5;
 (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5;
 (enoxaparin) 9041-08-1; (fondaparinux) 104993-28-4,
 114870-03-0; (warfarin) 129-06-6, 2610-86-8, 3324-63-8,
 5543-58-8, 81-81-2; (hirulog) 128270-60-0; (argatroban)
 74863-84-6; (ximelagatran) 192939-46-1, 260790-58-7;
 (streptokinase) 9002-01-1; (reteplase) 133652-38-7;
 (tenecteplase) 191588-94-0; (alteplase) 105857-23-6

CHEMICAL NAME: Aspirin

ACCESSION NUMBER: 2005-778298 [79] WPIX
 DOC. NO. CPI: C2005-238563
 TITLE: New fused heterocyclic compounds are potassium channel function inhibitors, useful to treat or prevent e.g. arrhythmias, atrial fibrillation, atrial flutter, supraventricular arrhythmias and chronic obstructive pulmonary disease.
 DERWENT CLASS: B02 B05
 INVENTOR(S): JOHNSON, J A; KOVER, A; LLOYD, J
 PATENT ASSIGNEE(S): (JOHN-I) JOHNSON J A; (KOVE-I) KOVER A; (LLOY-I) LLOYD J; (BRIM) BRISTOL-MYERS SQUIBB CO
 COUNTRY COUNT: 110
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
US 2005250783	A1	20051110	(200579)*		47	A61K031-501	
WO 2005105096	A2	20051110	(200579)	EN		A61K031-501	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW							

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2005250783	A1 Provisional	US 2004-563143P	20040415
		US 2005-104856	20050413
WO 2005105096	A2	WO 2005-US12542	20050414

PRIORITY APPLN. INFO: US 2004-563143P 20040415; US
 2005-104856 20050413

INT. PATENT CLASSIF.:

MAIN: A61K031-501
 SECONDARY: A61K031-416; A61K031-4172; A61K031-42; A61K031-433;
 A61K031-517

BASIC ABSTRACT:

US2005250783 A UPAB: 20051208
 NOVELTY - Fused heterocyclic compounds (I) and their salts, solvates and prodrugs, are new.
 DETAILED DESCRIPTION - Fused heterocyclic compounds of formula (I) and their salts, solvates and prodrugs, are new.
 n, m = integers such that ring H, including its fusion partner, is 5-7 membered;
 A, B1, D, E = -CR6=, -CR6-, -C(=O)-, -NR7-, -N=, -O-, -S-, bond or double bond;
 G (including atoms shared with its fusion partner) = 5-6 membered ring;
 R1 = aryl (optionally substituted by one or more -(CH2)p-(Z1)q-(CH2)r-Z2);
 R2 = aryl, heteroaryl, cycloalkyl or heterocyclo (all optionally substituted with one or more -(CH2)p-(Z1)q-(CH2)r-Z2) (substituents may join to form an optionally substituted carbocycle or heterocycle);
 Y = -C(=O), -C(=S)-, C(=NR9)-, -C(=NR10)NR11-, -C(=O)-O-, -C(=S)-O-,

-C(=NR12), -SO2- or single bond; either
 R3-R12 = -(CH2)p-(Z1)q-(CH2)r-Z2; or
 two R3-R5 = form optionally substituted carbocycle or heterocycle; or
 two R6 = phenyl (optionally substituted); or
 R6 and R7 = form optionally substituted carbocycle or heterocycle;
 Z1 = alkyl, alkenyl, alkynyl, carbocyclo, aryl, heterocyclo (all optionally substituted), -CZ3Z4-, -O-, -NZ5-, -S-, -SO-, -SO2-, -C(O)-, -C(O)Z6-, -C(O)NZ7-, -C(S)- or -C(=NOZ8)-; either
 Z2 = alkyl, alkenyl, alkynyl, carbocyclo, aryl, heterocyclo (all optionally substituted), H, -OZ9, -OC(O)Z10, -NZ11-CO-Z12, -NZ13-CO2-Z14, -NZ15(CO)-NZ16Z17, -NZ18Z19, -NO2, halo, -CN, -C(O)Z20, CO2Z21, -C(S)Z22, -C(=NOZ23)Z24, -C(O)NZ25Z26, -C(S)NZ27Z28, -SZ29, -SOZ30, -SO2Z31 or -SO2NZ32Z33; or
 NZ2Z5 = optionally substituted heterocycle;
 Z5 = alkyl, alkenyl, alkynyl, carbocyclo, aryl, heterocyclo, heteroaryl, (all optionally substituted), H, -C(O)Z20, -CO2Z21, -C(S)Z22, -C(=NOZ23)Z24, -C(O)NZ25Z26, -C(S)NZ27Z28, -SZ29, -SOZ30, -SO2Z31 or -SO2NZ32Z33;
 Z3, Z4, Z6-Z33 = alkyl, alkenyl, alkynyl, carbocyclo, aryl, heterocyclo (all optionally substituted), H or halo; or
 (MK#16) p, r = 0-10; and
 (MK#17) q = 0-1.

Provided that:

(1) ring G is a heterocycle, where at least one ring atom is nitrogen, and ring G and -C(=O)-, if present, contains at least one unsaturated bond; and

(2) when q is 0, r is also 0.

INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition (A) comprising (I), vehicle or carrier; and

(2) preparation of (I).

ACTIVITY - Antiarrhythmic; Gastrointestinal-Gen.; Antiinflammatory; Immunomodulator; Respiratory-Gen.; Antidiabetic; Nootropic; Antimigraine; Anticonvulsant; Hypotensive; Cardiant; Vasotropic; Antianginal; Laxative; Antidiarrheic; Antiasthmatic; Antiarthritic; Antirheumatic; Immunosuppressive; CNS-Gen.; Antiarteriosclerotic; Cytostatic; Ophthalmological; Nephrotropic; Neuroprotective; Antiparkinsonian; Muscular-Gen.; Antiulcer; Auditory; Dermatological; Antiallergic.

MECHANISM OF ACTION - Potassium channel function inhibitor; Ultra-rapidly activating delayed rectifier K⁺ current blocker. No biological data given.

USE - (I) are useful to treat or prevent arrhythmias, atrial fibrillation, atrial flutter and supraventricular arrhythmias. (I) are useful to treat gastrointestinal disorders (reflux esophagitis or motility disorder), inflammatory, immunological disease (chronic obstructive pulmonary disease), diabetes, cognitive disorder, migraine, epilepsy, hypertension and ultra-rapidly activating delayed rectifier K⁺ current (I-Kur) associated conditions; and to control heart rate (all claimed). (I) are useful to treat or prevent e.g. diabetes, cognitive disorders, migraine, epilepsy, hypertension, complications of cardiac ischemia, angina pectoris including relief of Prinzmetal's symptoms, vasospastic symptoms and variant symptoms; gastrointestinal disorders including reflux esophagitis, functional dyspepsia, motility disorders (including constipation and diarrhea), and irritable bowel syndrome, asthma, adult respiratory distress syndrome, peripheral vascular disease (including intermittent claudication), venous insufficiency, impotence, inflammatory bowel disease, rheumatoid arthritis, graft rejection, cystic fibrosis, atherosclerosis, restenosis, cancer, auditory system disorder, diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, Alzheimer's disease, dementia, central nervous system mediated motor dysfunction

including Parkinson's disease and ataxia; epilepsy; type I diabetes, uveitis, juvenile-onset or recent-onset diabetes mellitus, posterior uveitis, allergic encephalomyelitis, glomerulonephritis, Crohn's disease, ulcerative colitis, migraine, Goodpasture's syndrome, hemolytic-uremic syndrome, diabetic nephropathy, multiple myositis, Guillain-Barre syndrome, Meniere's disease, cutaneous T cell lymphoma, arteriosclerosis, aortitis syndrome, polyarteritis nodosa, myocardosis, scleroderma, Wegener's granuloma and Sjogren's syndrome.

ADVANTAGE - (I) improves cognition in animal models. (I) improves cognition and/or treating cognitive disorders.

Dwg.0/0

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; GI; DCN

MANUAL CODES: CPI: B01-B01; B02-D; B04-C01B; B04-C02E1; B04-C02X; B04-H15; B04-H1500E; B04-L05C; B04-N04A; B05-A03B; B05-B01E; B06-H; B07-H; B10-A08; B10-A17; B10-B02E; B10-C03; B14-C01; B14-C03; B14-C09B; B14-E02; B14-E09; B14-E10; B14-F01A; B14-F01D; B14-F01E; B14-F01G; B14-F02; B14-F07; B14-G02C; B14-G02D; B14-G03; B14-H01; B14-J01; B14-J07; B14-K01; B14-N02; B14-N03; B14-N10; B14-N16; B14-N17; B14-P02; B14-S04; B14-S16

TECH UPTX: 20051208

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation (claimed): Preparation of (I) comprises cyclizing a cyclopentane compound of formula (II) via one or more ring-forming reactions to give (I).

J = oxo or -OZ; and

Z = leaving group.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (A) further comprises at least one other therapeutic agent (anti-arrhythmic agent, calcium channel blocker, anti-platelet agent, antihypertensive agent, anti thrombotic/anti thrombolytic agent, anti coagulant, 5-hydroxy-1-methylglutaryl (HMG)-CoA reductase inhibitor, anti diabetic agent, thyroid mimetic, mineralocorticoid receptor antagonist or cardiac glycoside). (A) additionally contains propafenone, carvedilol, propranolol, sotalol, dofetilide, amiodarone, azimilide, ibutilide, diltiazem, verapamil, sulamserod, serraline, tropsetron, dronedarone, diltiazem, verapamil, nifedipine, amlodipine, mybefradil, aspirin, indomethacin, ibuprofen, piroxicam, naproxen, celebrex, viox, abciximab, eptifibatide, tirofiban, clopidogrel, cangrelor, ticlopidine, CS-747, ifetroban, aspirin, dipyridamole, chlorothiazide, hydrochlorothiazide, flumethiazide, hydroflumethiazide, bendroflumethiazide, methylchlorothiazide, trichloromethiazide, polythiazide, benzthiazide, ethacrynic acid, tricrynafene, chlorthalidone, furosemide, musolimine, bumetanide, triamtrenene, amiloride, spironolactone, captopril, zofenopril, fosinopril, enalapril, ceranopril, cilazopril, delapril, pentopril, quinapril, ramipril, lisinopril, losartan, irbesartan, valsartan, sitaxsentan, atrisentan, omapatrilat, gemopatrilat, nitrates, tPA, recombinant tPA, tenecteplase (TNK), lanoteplase (nPA), razaxaban, hirudin, argatroban, streptokinase, urokinase, prourokinase, anisoylated plasminogen streptokinase activator complex, warfarin, heparins (including unfractionated, low molecular weight heparins such as enoxaparin, dalteparin), pravastatin, lovastatin, atorvastatin, simvastatin, NK-104, ZD-4522, squalene, questran, cyclosporin A, taxol, FK 506, adriamycin, epothilones, cisplatin, carboplatin, metformin, acarbose, insulins, repaglinide, glimepiride, glyburide, glipizide, biguanide/glyburide combinations, troglitazone, rosiglitazone, pioglitazone, PPARgamma agonists, aP2 inhibitors, thyrotropin, polythyroid, KB-130015, eplerenone, alendronate, raloxifene, estrogen (including conjugated estrogens in premarin, estradiol),

nefazodone, sertraline, diazepam, lorazepam, buspirone, hydroxyzine pamoate, famotidine, ranitidine, omeprazole, orlistat, digitalis, ouabain, cilostazol, sildenafil, prednisone, dexamethasone or enbrel.

L53 ANSWER 55 OF 56 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2004-821596 [81] WPIX
 DOC. NO. CPI: C2004-285648
 TITLE: Treatment or prevention of cardiovascular diseases involves administering 2-acetoxy-5-(alpha-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno(3,2-c)pyridine, and performing **percutaneous coronary** intervention procedure.
 DERWENT CLASS: B02
 INVENTOR(S): BRANDT, J; FARID, N; JAKUBOWSKI, J; WINTERS, K; BRANDT, J T; FARID, N A; JAKUBOWSKI, J A; WINTERS, K J
 PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI
 COUNTRY COUNT: 109
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2004098713	A2	20041118	(200481)*	EN	31	A61P009-00	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW							
EP 1660183	A2	20060531	(200636)	EN		A61P009-00	
R: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LU MC NL PL PT RO SE SI SK TR							

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004098713	A2	WO 2004-US11257	20040426
EP 1660183	A2	EP 2004-750031	20040426
		WO 2004-US11257	20040426

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1660183	A2 Based on	WO 2004098713

PRIORITY APPLN. INFO: US 2003-467903P 20030505

INT. PATENT CLASSIF.:

MAIN: A61P009-00

SECONDARY: A61K031-4365; A61K031-60

BASIC ABSTRACT:

WO2004098713 A UPAB: 20041216

NOVELTY - Treatment or prevention of cardiovascular diseases and their recurrence involves administration of 2-acetoxy-5-(alpha-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno(3,2-c)pyridine (I) optionally in combination with **aspirin**; performing a **percutaneous coronary** intervention (PCI) procedure; and optionally administering (I) optionally in

combination with **aspirin**.

DETAILED DESCRIPTION - Treatment or prevention of cardiovascular diseases and their recurrence involves administration of 2-acetoxy-5-(alpha -cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno(3,2-c)pyridine (I), its salt, solvate, active metabolite, prodrug, racemate or enantiomer, optionally in combination with **aspirin**; performing a **percutaneous coronary intervention (PCI)** procedure; and optionally administering (I) optionally in combination with **aspirin**.

INDEPENDENT CLAIMS are included for the following:

- (1) a device coated or impregnated with (I);
- (2) use of (I) in conjunction with a **stent** for treating or preventing recurrence of peripheral vascular disease and cerebrovascular disease; and
- (3) treatment and prevention of cardiovascular disease and its recurrence involving administering (I), in combination with a **stent** impregnated with (I) and/or other cardio-protective agent.

ACTIVITY - Cardiovascular-Gen.; Vasotropic; Cardiant; Antiinflammatory; Antiarrhythmic.

MECHANISM OF ACTION - None given.

USE - In the manufacture of a medicament for treating or preventing the recurrence of cardiovascular disease e.g. coronary occlusion, restenosis, acute coronary syndrome, high risk vascular diseases, congestive heart failure, cardiac alternation, ventricular aneurysm, mural aneurysm, myocardial infarction, cardiac arrest, cardiac dysrhythmia including atrial fibrillation, cardiac edema, cardiac dyspnea, cardiac failure, tachycardia, cardiac hemoptysis, cardiac incompetence, cardiac murmur, cardiac syncope, cardiac tamponade, cerebrovascular disease and peripheral artery disease (claimed).

ADVANTAGE - The method improves or augments the efficiency of interventional procedures including stenting and balloon angioplasty to minimize recurrences and repeated interventions.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B06-F03; B10-C04B
TECH UPTX: 20041216

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: (m1) involves administration of (I), optionally in combination with **aspirin** or other cardio protective agent to 2 - 30 days prior to performing the **PCI** procedure; performing **PCI** procedure; and administering (I) optionally in combination with **aspirin** or other cardio protective agent to 0 - 365 days after performance of the **PCI** procedure.

L53 ANSWER 56 OF 56 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-482984 [52] WPIX
CROSS REFERENCE: 2000-170974 [15]
DOC. NO. CPI: C2001-144714
TITLE: New biphenyl sulfonamides, useful as angiotensin endothelin receptor antagonists and for treatment of e.g. hypertension, atherosclerosis, asthma and ischemia.
DERWENT CLASS: B05
INVENTOR(S): GU, Z; MACOR, J E; MURUGESAN, N; TELLEW, J E
PATENT ASSIGNEE(S): (BRIM) BRISTOL-MYERS SQUIBB CO
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG MAIN IPC
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WO 2001044239 A2 20010621 (200152)* EN 286 C07D413-12
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE
 ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
 LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK
 SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2001020926 A 20010625 (200162) C07D413-12
 EP 1237888 A2 20020911 (200267) EN C07D413-12
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR
 JP 2003520785 W 20030708 (200347) 346 C07D261-10

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001044239	A2	WO 2000-US33730	20001213
AU 2001020926	A	AU 2001-20926	20001213
EP 1237888	A2	EP 2000-984282	20001213
		WO 2000-US33730	20001213
JP 2003520785	W	WO 2000-US33730	20001213
		JP 2001-544729	20001213

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001020926	A Based on	WO 2001044239
EP 1237888	A2 Based on	WO 2001044239
JP 2003520785	W Based on	WO 2001044239

PRIORITY APPLN. INFO: US 2000-643640 20000822; US
 1999-464037 19991215; US
 2000-481197 20000111; US
 2000-513779 20000225; US
 2000-604322 20000626

INT. PATENT CLASSIF.:

MAIN: C07D261-10; C07D413-12
 SECONDARY: A61K031-42; A61K031-422; A61K031-4245; A61K031-433;
 A61K031-437; A61K031-4439; A61K031-454; A61K031-4709;
 A61K031-496; A61K031-497; A61K031-517; A61P003-10;
 A61P007-00; A61P009-04; A61P009-08; A61P009-10;
 A61P009-12; A61P011-00; A61P011-06; A61P013-08;
 A61P013-12; A61P015-10; A61P015-12; A61P025-06;
 A61P035-00; A61P043-00; C07D261-16; C07D401-12;
 C07D403-14; C07D413-14; C07D417-12; C07D417-14;
 C07D471-04; C07D487-04

BASIC ABSTRACT:

WO 2001044239 A UPAB: 20030723

NOVELTY - Biphenyl sulfonamides (I), and their enantiomers, diastereomers, salts and metabolites, are new.

DETAILED DESCRIPTION - Biphenyl sulfonamide compounds of formula (I), and their enantiomers, diastereomers, salts and metabolites, are new.

R1 = a group of formulae (a) - (o);

R2 = T or aryloxy, provided that when R1 is a group of formula (b), that R2 is not H, halo, (halo)alkyl, alkoxy, hydroxyalkyl, nitro, -(CH2)wNR19R20 or -NHSO2R22;

T = H, halo, CHO, (halo)alkyl, alkenyl, alkynyl, (halo)alkoxyalkyl, (cycloalkyl)alkyl, alkoxyalkoxy, cyano, hydroxy(alkyl), nitro,

-CH(OR13)(OR14) or -(CH2)wY

R3 = heteroaryl;

R4, R5 = (hydroxy)alkyl, (hydroxy-substituted)cycloalkyl or (hydroxy-substituted)alkoxyalkyl; or

R4 and R5 together = cyclobutyl, cyclopentyl, cyclohexyl, tetrahydrofuran-2-yl or tetrahydropyran-2-yl (all optionally substituted with one or more OH);

R6 = (hydroxy)(halo)alkyl, (hydroxy-substituted)(cycloalkyl)alkyl, aralkyl, (hydroxy-substituted)alkoxy(alkyl) or -NR16R17;

R7 = -(CH2)w-CO2R15, -(CH2)w-(C=O)NR16R17, -(CH2)w-NR15(C=O)NR16R17, -(CH2)w-CH2OH or -(CH2)w-(C=O)R15, or tetrazolyl, oxadiazolyl or triazolyl (each optionally substituted with H, alkyl, OH or halo);

R8, R9, R9a, R10, R12 = H, halo, (hydroxy)alkyl, (cycloalkyl)(alkyl), (hetero)aryl, arylalkyl, alkylthioalkyl, alkoxy(alkyl); or

R11, R11a = H, alkoxy or together form a carbonyl;

R13, R14 = alkyl or together form a 5- or 6-membered ring;

R15, R16, R17 = H, (hydroxy)alkyl, (cycloalkyl)(alkyl), alkoxyalkyl, aralkyl, heterocycloalkyl, (hetero)aryl or -(CH2)wQ; or

R16 and R17 together = 4-6 membered heterocyclic ring;

n = 1 or 2;

w = 0, 1 or 2;

Y = heteroaryl, -COOH, -COOR18, -CONR19R20, -NR19-OR20, -NR21(C=O)R22, -NR21(C=O)NR19R20, -N(R19)-(alk)-NR21(C=O)R22, -NR21(C=O)OR18, -NR21SO2R22, -SO2R22, or a group of formulae (q), (r) or (s);

R18 - R22 = H, (halo)alkyl, alkoxyalkyl, cycloalkyl, alkenyl, alkynyl, (hetero)aryl or aralkyl; or

R19 and R20 together = 4-7 membered cycloalkyl ring;

R23, R24 = H, (cyclo)alkyl or together form a 3-7 membered ring;

Z = O, -N(R25)- or -C(R26)(R27)-;

x = 2, 3 or 4;

R25, R26, R27 = H, (cyclo)alkyl or R26 and R27 together form a 3-7 membered cycloalkyl ring; and

R101 - R104 = T in which all (hetero)aryl rings are optionally substituted by H, halo, cyano, (hydroxy)alkyl, alkoxy, nitro or trifluoromethyl.

Provided that when R1 is a group of formula (a), (I) is not a compound of formula (II).

INDEPENDENT CLAIMS are also included for:

(1) a compound of formula (I) in which R3 = isoxazol-5-yl or isoxazol-3-yl (optionally substituted with 2 of alkyl or halogen, and R1 is any group such that the resulting compound demonstrates affinity (IC50) for both the AT1 receptor and ETA receptor of less than 5 mM at both receptors

(2) a pharmaceutical composition comprising (I), at least one ACE inhibitor (such as captopril, zofenopril, fosinopril, ceranopril, alacepril, enalapril, delapril, pentopril, quinopril, ramipril, or lisinopril), vasopeptidase inhibitor (such as omapatrilat or gemopatrilat), HMG CoA reductase inhibitor (such as pravastatin, lovastatin, atorvastatin, simvastatin, NK-104 or ZD-4522), anti-platelet agent (such as clopidogrel, ticlopidine, CS-747 or aspirin), anti-diabetic agent (such as biguanides or biguanide/glyburide combinations), beta-adrenergic agent (such as carvedilol or metoprolol) or mineralocorticoid receptor antagonist (such as spironolactone or eplerenone).

ACTIVITY - Antiarthritic; neuroprotective; antianalgesic; antiarrhythmic; antiarteriosclerotic; antiinflammatory; analgesic; cytostatic; cardiant; cerebroprotective; hepatotropic; dermatological; ophthalmological; antidiabetic; antidiarrheic; anticonvulsant; vasotropic; litholytic; hemostatic; hypotensive; antimigraine; osteopathic;

antipsoriatic; antiulcer.

MECHANISM OF ACTION - Endothelin receptor antagonist; angiotensin II receptor antagonist. Tests were carried out but no results are given.

USE - (I) are useful in the treatment of disorders related to renal, glomerular and mesangial cell function. For treatment of disorders related to paracrine and endocrine function. For treatment of endotoxemia or endotoxin shock or hemorrhagic shock. For alleviating pain associated with prostate and bone cancer. For preventing end-organ damage associated with the cell-proliferative effects of endothelin. For treatment of hypoxic and ischemic diseases (such as cardiac, renal and cerebral ischemia and reperfusion). As antiarrhythmic, antianginal, antifibrillatory, antiasthmatic, antiarteriosclerotic, and antidiarrheal agents. As adjuncts to thrombolytic therapy. For treatment of myocardial infarction, peripheral vascular disease (e.g. Raynaud's disease), cardiac hypertrophy, primary pulmonary hypertension, trauma, central nervous system vascular disorders (such as migraine, stroke and hemorrhage), central nervous system behavioural disorders, gastrointestinal diseases (such as Crohn's disease, ulcers and inflammatory bowel disease), pancreatitis and gall bladder disorders. For regulation of cell growth. For treatment of restenosis following transplantation. For therapy of congestive heart failure including inhibition of fibrosis. For treatment of sickle cell disease, liver disease, deleterious consequences of ET-producing tumors, spastic diseases of the urinary tract and bladder, hepatorenal syndrome, immunological diseases (including vasculitis) fibrosis associated with renal dysfunction, metabolic and neurological disorders, cancer, insulin-retinopathy, diabetes mellitus, neuropathy, retinopathy, epilepsy, bone remodelling, psoriasis, and chronic inflammatory diseases (such as arthritis, rheumatoid arthritis, osteoarthritis, sarcoidosis and eczematous dermatitis). For treatment of disorders involving bronchoconstriction. For treatment of sexual dysfunction, Alzheimer's, senile dementia and vascular dementia.

Dwg.0/0

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; GI; DCN

MANUAL CODES: CPI: B05-B01E; B06-H; B07-D04B; B07-D09; B07-D13;
B10-A08; B10-A17; B10-B02B; B10-C03; B14-C09;
B14-E02; B14-E10; B14-F01; B14-F02B; B14-F02C;
B14-F02D; B14-F03; B14-F07; B14-G02C; B14-G03;
B14-H01; B14-J01; B14-J05D; B14-J07; B14-K01A;
B14-K01D; B14-N01; B14-N13; B14-N16; B14-S06;
B14-S07

TECH UPTX: 20010914

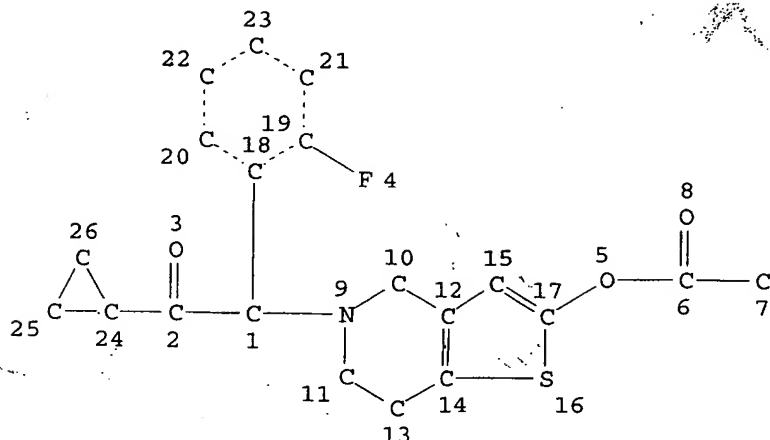
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) can be prepared by:

- (1) reacting a sulfonyl-substituted phenyl bromide with an phenyl boronic acid (or ester) to form a biphenyl sulfonyl compound;
- (2) converting the biphenyl sulfonyl compound into a biphenyl sulfonyl chloride; and
- (3) reacting the biphenyl sulfonyl chloride compound with an aryl amine.

FILE 'HOME' ENTERED AT 11:48:04 ON 10 AUG 2006

=>

=> d stat que l19; d his nofile
L17 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
L19 3 SEA FILE=REGISTRY FAM FUL L17

100.0% PROCESSED 14 ITERATIONS
SEARCH TIME: 00.00.01

3 ANSWERS

(FILE 'HOME' ENTERED AT 11:14:07 ON 10 AUG 2006)

FILE 'CAPLUS' ENTERED AT 11:16:02 ON 10 AUG 2006
E US2005-553763/APPS

L1 558 SEA ABB=ON BRANDT J?/AU
L2 152 SEA ABB=ON FARID N?/AU
L3 261 SEA ABB=ON JAKUBOWSKI J?/AU
L4 89 SEA ABB=ON WINTERS K?/AU
L5 2 SEA ABB=ON L1 AND L2 AND L3 AND L4
D SCAN TI
D SCAN
SEL RN

FILE 'REGISTRY' ENTERED AT 11:17:20 ON 10 AUG 2006

L6 10 SEA ABB=ON (115473-15-9/BI OR 150322-38-6/BI OR 150322-43-3/BI
OR 150322-73-9/BI OR 204205-33-4/BI OR 389574-19-0/BI OR
389574-20-3/BI OR 446-48-0/BI OR 50-78-2/BI OR 5500-21-0/BI)
D SCAN
L7 1 SEA ABB=ON C20 H20 F N O3 S/MF AND L6
D SCAN

FILE 'STNGUIDE' ENTERED AT 11:19:02 ON 10 AUG 2006

Searched by Barb O'Bryen, STIC 2-2518

FILE 'MEDLINE, JICST-EPLUS, WPIX, BIOSIS, EMBASE' ENTERED AT 11:20:45 ON
10 AUG 2006

L8 2404 SEA ABB=ON BRANDT J?/AU
L9 772 SEA ABB=ON FARID N?/AU
L10 629 SEA ABB=ON JAKUBOWSKI J?/AU
L11 371 SEA ABB=ON WINTERS K?/AU
L12 55838 SEA ABB=ON PERCUTANEOUS?(5A) CORONARY
L13 3 SEA ABB=ON L8 AND L9 AND L10 AND L11
L14 16 SEA ABB=ON (L8 OR L9 OR L10 OR L11) AND L12

FILE 'CAPLUS' ENTERED AT 11:22:03 ON 10 AUG 2006
D QUE L5

FILE 'MEDLINE, JICST-EPLUS, WPIX, BIOSIS, EMBASE' ENTERED AT 11:22:14 ON
10 AUG 2006

D QUE L13
D QUE L14
L15 18 SEA ABB=ON L13 OR L14

FILE 'CAPLUS, MEDLINE, WPIX, BIOSIS, EMBASE' ENTERED AT 11:22:19 ON 10
AUG 2006

L16 13 DUP REM L5 L15 (7 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE CAPLUS
ANSWERS '3-7' FROM FILE MEDLINE
ANSWERS '8-13' FROM FILE BIOSIS
D IBIB ED ABS 1-2
D IALL 3-13

FILE 'REGISTRY' ENTERED AT 11:22:50 ON 10 AUG 2006
D IDE L7

L17 STR 150322-43-3
L18 0 SEA FAM SAM L17
L19 3 SEA FAM FUL L17
SAVE TEMP L19 GEM763FAM/A
D LC 1-3

FILE 'CAPLUS' ENTERED AT 11:25:18 ON 10 AUG 2006

L20 27 SEA ABB=ON L19

FILE 'IPA, BIOSIS, EMBASE, TOXCENTER, IMSRESEARCH, PROUSDDR' ENTERED AT
11:26:02 ON 10 AUG 2006

L21 61 SEA ABB=ON L19

FILE 'CAPLUS, IPA, BIOSIS, EMBASE, TOXCENTER, IMSRESEARCH, PROUSDDR'
ENTERED AT 11:26:12 ON 10 AUG 2006

L22 71 DUP REM L20 L21 (17 DUPLICATES REMOVED)
ANSWERS '1-27' FROM FILE CAPLUS
ANSWER '28' FROM FILE IPA
ANSWERS '29-34' FROM FILE BIOSIS
ANSWERS '35-67' FROM FILE EMBASE
ANSWERS '68-69' FROM FILE TOXCENTER
ANSWER '70' FROM FILE IMSRESEARCH
ANSWER '71' FROM FILE PROUSDDR

FILE 'IPA, BIOSIS, TOXCENTER, IMSRESEARCH, PROUSDDR' ENTERED AT 11:27:04
ON 10 AUG 2006

L23 27 SEA ABB=ON L19

FILE 'CAPLUS, IPA, BIOSIS, TOXCENTER, IMSRESEARCH, PROUSDDR' ENTERED AT

BI, ABEX
L40 8483 SEA ABB=ON STENT#/BI, ABEX
L41 4848 SEA ABB=ON PCI/BI, ABEX OR (PERCUTANEOUS?/BI, ABEX OR PER
CUTANEOUS?/BI, ABEX OR TRANSLUMINAL?/BI, ABEX OR TRANS LUMINAL?/B
I, ABEX) (5A) CORONARY/BI, ABEX
L42 9 SEA ABB=ON L37 AND (L39 OR L40 OR L41)

FILE 'WPIX' ENTERED AT 11:41:03 ON 10 AUG 2006
D QUE L42

FILE 'CAPLUS, IPA, BIOSIS, TOXCENTER, IMSRESEARCH, PROUSDDR, WPIX,
EMBASE' ENTERED AT 11:41:31 ON 10 AUG 2006
L43 63 DUP REM L34 L23 L42 L33 (22 DUPLICATES REMOVED)
ANSWERS '1-26' FROM FILE CAPLUS
ANSWER '27' FROM FILE IPA
ANSWERS '28-33' FROM FILE BIOSIS
ANSWERS '34-35' FROM FILE TOXCENTER
ANSWER '36' FROM FILE IMSRESEARCH
ANSWER '37' FROM FILE PROUSDDR
ANSWERS '38-40' FROM FILE WPIX
ANSWERS '41-63' FROM FILE EMBASE

FILE 'CAPLUS' ENTERED AT 11:42:12 ON 10 AUG 2006
D SCAN L5

FILE 'REGISTRY' ENTERED AT 11:42:38 ON 10 AUG 2006
L44 1 SEA ABB=ON ASPIRIN/CN

FILE 'CAPLUS' ENTERED AT 11:42:43 ON 10 AUG 2006
L45 20321 SEA ABB=ON L44
L46 4141 SEA ABB=ON STENT#/OBI
L47 7059 SEA ABB=ON (PCI OR (PERCUTANEOUS? OR PER CUTANEOUS? OR
TRANSLUMINAL? OR TRANS LUMINAL?) (5A) CORONARY) /BI
D QUE NOS L20
L48 12 SEA ABB=ON L20 AND (L45 OR L46 OR L47)
L49 15 SEA ABB=ON L20 NOT (L48 OR L5)
D SCAN TI
L50 1 SEA ABB=ON L49 AND COATINGS/TI
D SCAN
L51 1 SEA ABB=ON L20 AND COATINGS/TI

FILE 'CAPLUS' ENTERED AT 11:46:37 ON 10 AUG 2006
D QUE NOS L48
D QUE NOS L51
L52 12 SEA ABB=ON (L48 OR L51) NOT L5

FILE 'CAPLUS, IPA, BIOSIS, TOXCENTER, IMSRESEARCH, PROUSDDR, EMBASE,
WPIX' ENTERED AT 11:47:14 ON 10 AUG 2006
L53 56 DUP REM L52 L23 L33 L42 (15 DUPLICATES REMOVED)
ANSWERS '1-12' FROM FILE CAPLUS
ANSWERS '13-14' FROM FILE IPA
ANSWERS '15-23' FROM FILE BIOSIS
ANSWERS '24-28' FROM FILE TOXCENTER
ANSWER '29' FROM FILE IMSRESEARCH
ANSWER '30' FROM FILE PROUSDDR
ANSWERS '31-53' FROM FILE EMBASE
ANSWERS '54-56' FROM FILE WPIX
D IBIB ED ABS HITSTR 1-12
D IALL 13-53
D IALL ABEQ TECH 54-56

11:27:32 ON 10 AUG 2006
L24 38 DUP REM L20 L23 (16 DUPLICATES REMOVED)
ANSWERS '1-27' FROM FILE CAPLUS
ANSWER '28' FROM FILE IPA
ANSWERS '29-34' FROM FILE BIOSIS
ANSWERS '35-36' FROM FILE TOXCENTER
ANSWER '37' FROM FILE IMSRESEARCH
ANSWER '38' FROM FILE PROUSDDR

FILE 'EMBASE' ENTERED AT 11:27:45 ON 10 AUG 2006
L25 34 SEA ABB=ON L19
D TRIAL 1-5
E CARDIOVASCULAR DISEASE+ALL/CT
L26 1218793 SEA ABB=ON CARDIOVASCULAR DISEASE+NT/CT
L27 14231 SEA ABB=ON PCI OR PERCUTANEOUS? (5A) CORONARY
D TRIAL 10000-10005
L28 13711 SEA ABB=ON TRANSLUMINAL CORONARY ANGIOPLASTY/CT
L29 26 SEA ABB=ON L25 AND (L26 OR L27 OR L28)
E ASPIRIN/CT
E E3+ALL
L30 82369 SEA ABB=ON ACETYLSALICYLIC ACID/CT
E STENT/CT
E E3+ALL
L31 27019 SEA ABB=ON STENT+NT/CT
L32 26 SEA ABB=ON L25 AND (L30 OR L31)
L33 23 SEA ABB=ON L25 AND (L30 OR L31) AND (L26 OR L27 OR L28)
D STAT QUE L19

FILE 'CAPLUS' ENTERED AT 11:35:07 ON 10 AUG 2006
D QUE NOS L20
L34 26 SEA ABB=ON L20 NOT L5

FILE 'EMBASE' ENTERED AT 11:35:07 ON 10 AUG 2006
D QUE NOS L33

FILE 'REGISTRY' ENTERED AT 11:35:12 ON 10 AUG 2006
D IDE L19 1-3

FILE 'CAPLUS' ENTERED AT 11:35:20 ON 10 AUG 2006
D QUE NOS L20
L35 26 SEA ABB=ON L20 NOT L5

FILE 'EMBASE' ENTERED AT 11:35:21 ON 10 AUG 2006
D QUE NOS L33

FILE 'IPA, BIOSIS, TOXCENTER, IMSRESEARCH, PROUSDDR' ENTERED AT 11:35:41
ON 10 AUG 2006
D QUE NOS L23

FILE 'WPIX' ENTERED AT 11:36:09 ON 10 AUG 2006
E PRASUGREL/CN
L36 1 SEA ABB=ON PRASUGREL/CN
D SDCN DCSE
L37 11 SEA ABB=ON RA7RM2/DCN OR 199852-0-0-0/DCRE OR PRASUGREL/BI,ABE
X OR CS747/BI,ABEX OR CS 747/BI,ABEX
E ASPIRIN/CN
L38 1 SEA ABB=ON ASPIRIN/CN
D SDCN DCSE
L39 4469 SEA ABB=ON R00034/DCN OR R06663/DCN OR 87874-0-0-0/DCRE OR
ASPIRIN/BI,ABEX OR ACETYLSALICYLIC/BI,ABEX OR ACETYL SALICYLIC/

FILE 'HOME' ENTERED AT 11:48:04 ON 10 AUG 2006
D STAT QUE L19

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